A. M. A.

ARCHIVES OF

DERMATOLOGY AND SYPHILOLOGY

EDITORIAL BOARD

PAUL A. O'LEARY, Chief Editor
102 Second Avenue S. W., Rochester, Minn.

HERBERT RATTNER, Associate Editor, Chicago

NELSON PAUL ANDERSON, Los Angeles
GEORGE M. LEWIS, New York
H. E. MICHELSON, Minneapolis
A. C. CIPOLLARO, New York
J. LAMAR CALLAWAY, Durham, N. C.

FEBRUARY 1953

VOLUME 67 NUMBER 2

Published Monthly by

AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

Entered as Second Class Matter Oct. 30, 1917, at the Postoffice at Chicago, Under the Act of March 3, 1879. Annual Subscription, $12.00

TABLE OF CONTENTS FIRST PAGE

A UNIT FOR EVERY DERMATOLOGICAL REQUIREMENT

BUCKY Therapy Apparatus

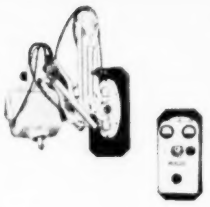
Completely mobile units . . . no installation needed

Wall-mounted units, tube holder arms and controls installed according to your specifications. Takes up no floor space.

Model T-1-B

X-RAY THERAPY APPARATUS

stepless range from 30-80 K.V.



Model T-2-A

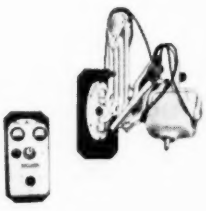
Model G-3

Originators of

COMBINATION THERAPY APPARATUS

one unit provides all three:
X-ray, Contact and Grenz Ray Therapy
Complete step-less radiation range (5-80 KV.) for skin therapy.

Three Units for the price of one



Model G-3W

Model G-2

GRENZ RAY THERAPY APPARATUS

Model G-2W

The International Medical Research Co.
60 East 42nd Street, New York 17, N. Y.

SALES and SERVICE in ALL MAJOR CITIES and COUNTRIES

Manufactured by The X-Ray Mfg. Corp. of America, New York, N.Y.

CONTENTS

Original Articles

Local Oxytetracycline ("Terramycin") Therapy of Skin Infections PAGE

Carroll S. Wright, M.D., and Donald N. Tschan, M.D., Philadelphia 125

Chromoblastomycosis

A. James French, M.D., Ann Arbor, Mich., and Sherwood R. Russell, M.D., St. Johns, Mich. 129

Nodular Vasculitis

S. Irgang, M.D., New York 135

Pregnenolone Acetate in the Treatment of Mycetoma (Nocardiosis)

John H. Lamb, M.D.; Florene C. Kelly, Ph.D.; Paul O. Shackelford, M.D.; Gerbert Rebell, and Rollin C. Koons, B.S., Oklahoma City 141

Eruptive Xanthoma and Hyperlipemia in Glycogen Storage Disease (von Gierke's Disease)

Samuel J. Zakon, M.D.; Abe Oyamada, M.D., and I. H. Rosenthal, M.D., Chicago 146

Bullous Keratogenous and Pigmentary Dermatitis with Blood Eosinophilia in Newborn Girls

G. Asboe-Hansen, M.D., Copenhagen, Denmark 152

Ultrasonic Vibrations

H. J. Templeton, M.D., Oakland, Calif. 158

Local Tissue Reactions to Cortisone and Hydrocortisone (Compound F) in Man

Leon Goldman, M.D., and Robert H. Preston, M.D., Cincinnati 163

Corticotropin (ACTH) and Cortisone in Treatment of Pemphigus Vulgaris

J. T. Aquilina, M.D.; James H. Townsend, M.D.; Ross Imburgia, M.D.; S. A. Greenstein, M.D., and R. L. Wuertz, M.D., Buffalo 166

The Acne Problem

Frederic T. Becker, M.D., Duluth, Minn. 173

Polyarteritis Nodosa and Dermatitis Gangrenosa

Captain Robert L. Gilman (MC), U.S.N., and Commander Karl V. Kaess (MC), U.S.N., Philadelphia 184

Amyloid "Tumor Formation" of the Skin

Irving N. Holtzman, M.D., and Jacob Skeer, M.D., Brooklyn 187

(Continued on Next Page)

CONTENTS—Continued

Effect of Roentgen Rays on Microsporum Audouini PAGE

Kurt Loewenthal, M.D., Freeport, N. Y. 191

Studies on Lichen Myxedematosus (Papular Mucinosis)

John Eric Dalton, M.D., and Martin A. Seidell, M.D., Indianapolis 194

Clinical Notes, New Instruments and Techniques

Rapid and Easy Method for Staining Spirochetes with Fountain Pen Ink

Edward T. Emura, M.D., Cincinnati 210

Electrodesiccation

Milton S. Hartman, M.D., Brooklyn 212

Society Transactions

Bronx Dermatological Society 214

New York Dermatological Society 220

Philadelphia Dermatological Society 226

Regular Departments

Directory of Dermatologic Societies 232

THE A. M. A. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY is published by the American Medical Association to stimulate research and to disseminate knowledge in these departments of medicine.

Communications regarding subscriptions, reprints, etc., should be addressed, A. M. A. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, American Medical Association, 535 North Dearborn Street, Chicago 10.

Manuscripts for publication, books for review and correspondence relating to the editorial management should be sent to Dr. Paul A. O'Leary, Chief Editor, 102 Second Avenue, S.W., Rochester, Minn., or to any other member of the Editorial Board.

Articles are accepted for publication on condition that they are contributed solely to the A. M. A. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. Manuscripts must be typewritten, preferably double spaced, and the original copy should be submitted. Zinc etchings and halftones will be supplied by the Association when the original illustrations warrant reproduction and when their number is not considered excessive.

Footnotes and bibliographies (the latter are used only in exhaustive reviews of the literature) should conform to the style of the *Quarterly Cumulative Index Medicus*. This requires, month—day of month if the journal appears weekly—and year.

Matter appearing in the A. M. A. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY is covered by copyright, but as a rule no objection will be made to its reproduction in a reputable medical journal if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the A. M. A. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY or in any of the other publications issued by the Association will not be permitted.

The A. M. A. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY is published monthly. The annual subscription price (for two volumes) is as follows: domestic, $12.00; Canadian, $12.40; foreign, $13.50, including postage. Current single copies are $1.25, postpaid.

Checks, money orders and drafts should be made payable to the American Medical Association.

Upjohn

less-antigenic penicillin:

Cer-O-Cillin

Trademark Reg. U. S. Pat. Off.

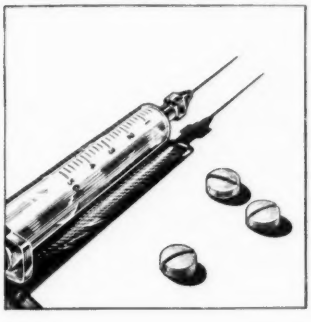
POTASSIUM

Available as:

Sterile vials containing 200,000 units Crystalline Penicillin O Potassium

Bottles of 12 buffered tablets, each containing 100,000 units Crystalline Penicillin O Potassium

The Upjohn Company, Kalamazoo, Michigan



Help for the "Confirmed Scratcher"[2] *with*

SENILE PRURITUS...

Partly by their low boiling fractions but mainly by their reducing action, tars exert their vasoconstrictor, astringent and antipruriginous qualities.[1] *They frequently provide welcome relief in senile pruritis, that "most annoying condition to plague the aged."*[2]

ALMAY Tar Bath—contains Juniper Tar (Oil of Cade) in a water-miscible base. Will not discolor skin, hair or bathtub. Two to four tablespoons required to the tub of water, in which body should be submerged for about 10 minutes. Room, water and towel should be at body temperature

Juniper Tar Ointment—greaseless, non-staining, water-miscible preparation containing Oil of Cade, 4%, in a bland base consisting of a potassium stearate cream and containing also stearin mono-glycerol ester, cetyl alcohol, propylene glycol and water. To be applied two to three times daily or whenever necessary to combat itching.

ALMAY®

DIVISION OF **Schieffelin & Co.**
22 COOPER SQUARE • NEW YORK 3, N. Y.

References:

1. Rothman, J. and Shapiro, A. L.: Med. Clin. N. Amer. 33:274-5, Jan., 1949.
2. Stieglitz, E. J.: Geriatric Medicine, p. 848, 1943.

ACCEPTED COMMITTEE ON COSMETICS AMERICAN MEDICAL ASSOCIATION

PAX-LANO-SAV . . . Heavy Duty carries the Official Seal of Acceptance of the Committee on Cosmetics of the American Medical Association.

PAX-LANO-SAV

Heavy Duty Granulated Skin Cleanser

helps STOP INDUSTRY'S "BIG ITCH"!

● *Industrial Dermatitis averages 10 weeks lost time plus $147 medical and compensation costs per case!*

AMAZING? Yes—but true, according to a survey recently conducted by OCCUPATIONAL HAZARDS. What's worse, dermatitis accounts for 60% of *all occupational disease cases* and almost 40% of *all occupational disease compensation*. It can cost you thousands of dollars a year!

THE FIRST STEP recommended to prevent dermatitis in this report is personal cleanliness, with special emphasis on *adequate washroom facilities* and *the right cleansers*. We quote:

> "If a harsh soap is used on hands that have been defatted by chemicals in the shop, the result will be *worse than if the worker had never washed*. So make sure that the soaps you provide in your washrooms are: 1) effective but harmless in themselves; 2) handily supplied so that they serve as reminders to use; 3) conveniently provided to eliminate mess and annoyance."

PAX-LANO-SAV *Heavy Duty* more than meets every requirement: (1) Years of experience in America's leading plants have proved its amazing cleansing ability . . . yet thanks to its rich formulation of lanolin and fine emollients usually found only in expensive creams and lotions, PAX-LANO-SAV *Heavy Duty* helps keep skin healthy despite work-contact irritants. (2) Workers *like* to use it—on face as well as hands—because it feels good, does not irritate the average skin, and they can *get clean quicker with less*. (3) PAX "Soap Saver" Dispensers supply it most conveniently, without fuss or muss.

Let PAX-LANO-SAV *Heavy Duty* help stop your "Big Itch"—and all the losses it causes . . .

Look for the PAX ROOSTER—It's your assurance of a Superior Product

PAX

The PAX trademark symbolizes a deep-rooted tradition of superlative quality maintained through a quarter century of continuous research and development.

LET US PROVE PAX IN YOUR WASHROOM...NOW!

Write today on your letterhead for a free half pound sample of PAX-LANO-SAV Heavy Duty Granulated Skin Cleanser. Then at your request our representative will gladly conduct a competitive test between PAX and your present brand—let you and your workers be the judge.

There is a complete line of PAX Skin Cleansers and Special Purpose Cleansers—each the finest in its price class.

ALL PRODUCT NAMES USED ARE TRADE NAMES OF THE G. H. PACKWOOD MFG. CO.

G. H. PACKWOOD MFG. CO. • 1537 TOWER GROVE AVE., ST. LOUIS 10, MO.

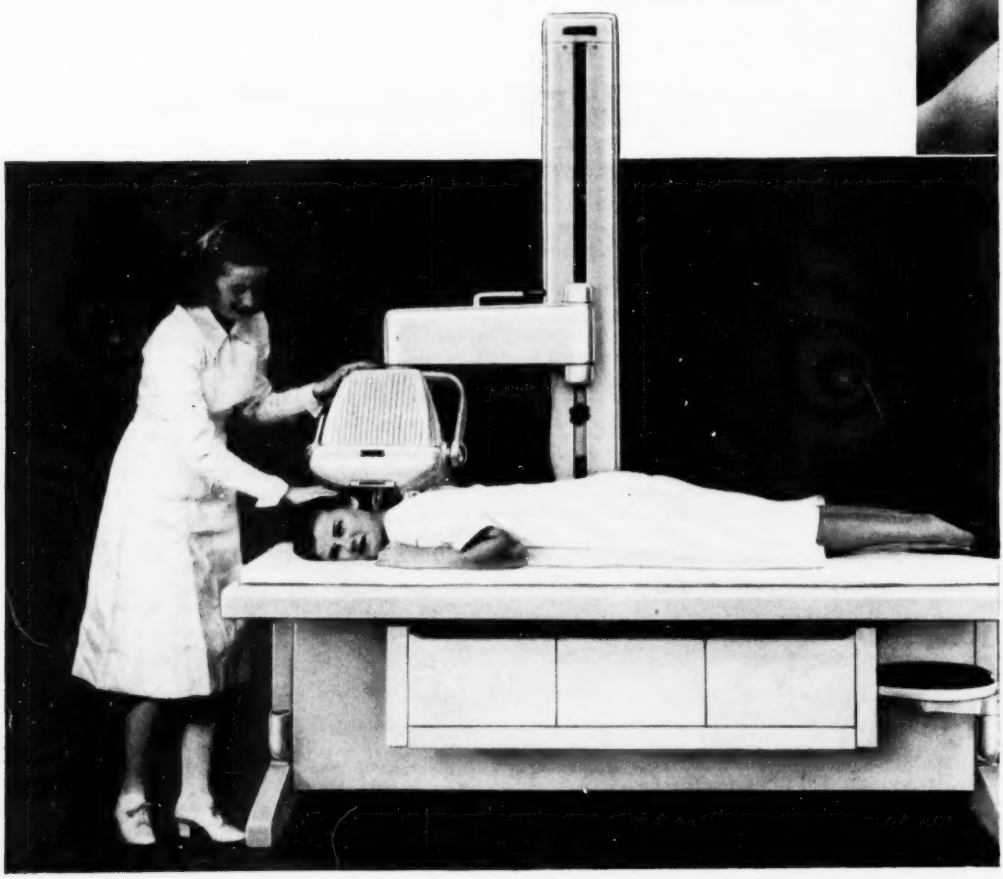
What is skin-deep?

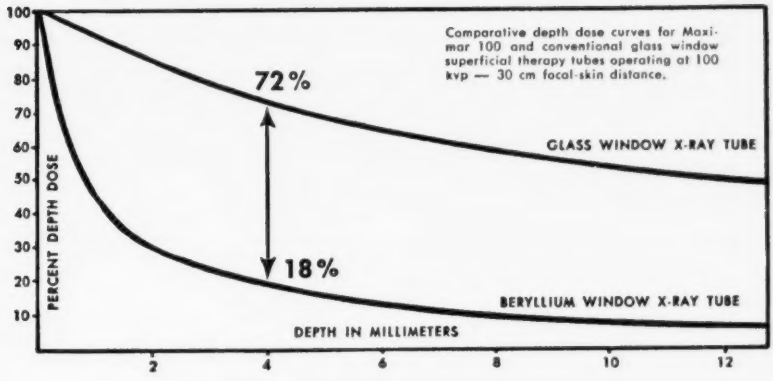
If you're talking superficial therapy — it's only about 4 mm. And that's where GE Maximar 100 delivers 82% of *its depth* dose!

It's GE's Coolidge tube with the beryllium window that makes the big difference between the Maximar 100 and other superficial therapy units. Thanks to the window's low inherent filtration, *the depth dose at 4 mm is only 18%.* As can be seen from the curves at the right, this compares with 72% for glass-window tube units.

In addition, Maximar 100 makes possible softer radiation at far higher intensities . . . with large field coverage. And precise, flexible control permits exact, uniform dosages . . . every time.

If you're considering the purchase of a superficial therapy unit, get all the facts about Maximar 100 from your GE x-ray representative. Or write X-Ray Department, General Electric Company, Milwaukee 1, Wisconsin, for Pub. P-2.





You can put your confidence in —

GENERAL ELECTRIC

Now...

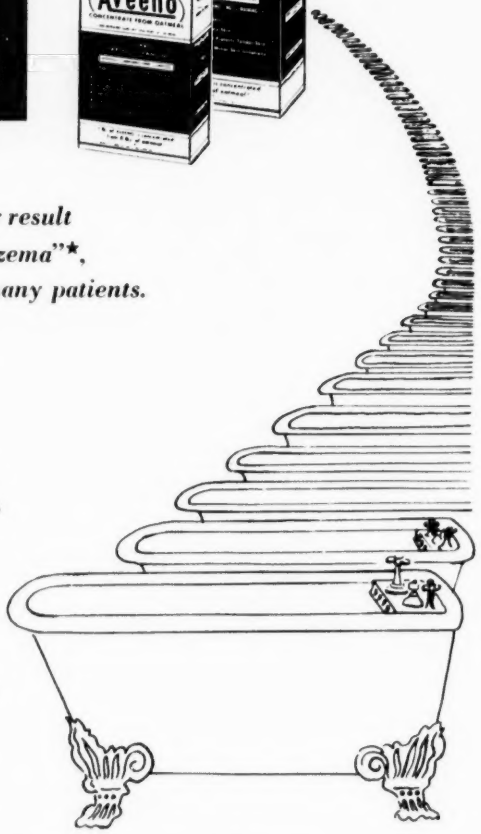
extensive bath schedules may be maintained without itching or skin irritation

Extensive bath schedules may result in a "bath itch" or "bath eczema"★, thus causing discomfort to many patients.

AVEENO, because of its colloidal nature and natural oil content, softens the skin and provides a soothing, lubricating action, thus permitting the patient to maintain regular bath schedules without irritation or pruritic effect.

In wet dressings for localized areas, as well as in colloid baths, Aveeno helps relieve irritated, inflamed or itching skin conditions. It also affords an excellent method for cleansing soap-sensitive and water-sensitive skin.

★ Sulzberger, M. B. and Baer, R. L.: Medical Uses of Soap, J. B. Lippincott Company, Philadelphia, 1946.



Send for professional samples and literature

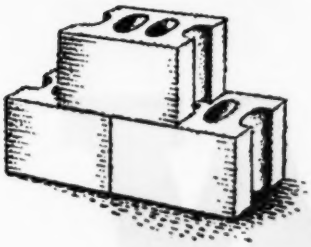
E. FOUGERA & CO., INC. • Distributors • 75 Varick St., New York 13, N. Y.

Product of Musher Foundation, Inc., New York, N. Y.

AVEENO®... concentrate from oatmeal for bland, soothing skin therapy

Available in Drug Stores only . . . in 18 oz. and 4 lb. packages

PRESCRIBE THE LARGE 4 LB. ECONOMY SIZE FOR EXTENSIVE BATH SCHEDULES



two basic
dermatologic
preparations...

WRIGHT'S®

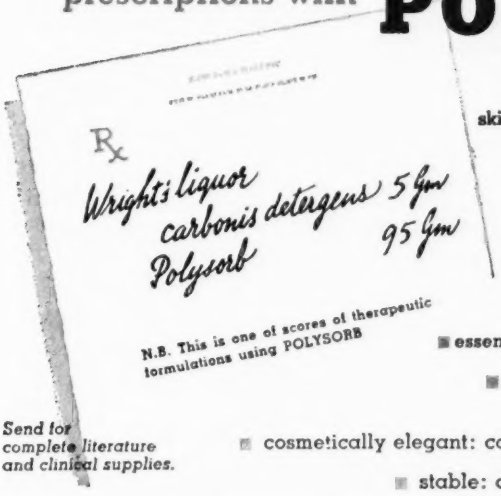
liquor carbonis detergens

a superior agent for **any** coal tar therapy...

- improved agent for time-tested coal tar therapy
- clears or greatly improves lesions even in refractory cases
- effective with or without ultra-violet irradiation
- application simple — applied undiluted with one-inch paint brush or as an ointment or lotion
- avoid unpleasant odors and tackiness of crude coal tar

WRIGHT'S LIQUOR CARBONIS DETERGENS is available in 3-oz., 8-oz. and 16-oz. bottles.

it's easy to write extemporaneous dermatologic prescriptions with **POLYSORB®...**


Rx
Wright's liquor carbonis detergens 5 Gm
Polysorb 95 Gm
N.B. This is one of scores of therapeutic formulations using POLYSORB

Write your Rx for any skin medication with POLYSORB Fougera versatile ointment vehicle

- complete: nothing to add but your medication
- compatible with all commonly used dermatologic agents
- essentially nonirritating, nonsensitizing, neutral pH
- water-miscible: readily washes off skin and hair
- cosmetically elegant: colorless, odorless, optimal "sheen" and "slip"
- stable: does not dry out or turn rancid

Send for complete literature and clinical supplies.

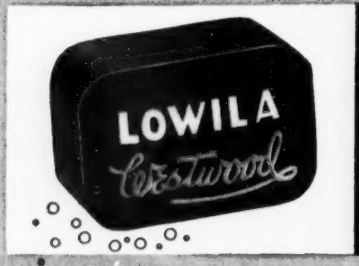
POLYSORB Fougera is available in 100 Gm. and 1 lb. jars; also in 5 lb. and 35 lb. bulk containers.
Sorbitan sesquioleate in balanced wax petrolatum mixture.

FOUGERA E. FOUGERA & CO., INC. 75 Varick Street, New York 13, N. Y.

*T.M.

totally
new
and improved
in every
way

...for cleansing the soap-sensitive skin



LOWILA® Cake

new rich, instant, abundant lather and excellent cleansing efficiency.

now stays firm to last bit, never crumbles, because of new hard-milling compression process.

new economy—**LOWILA** costs less than any other soap substitute for personal use.

super-mild, soapless—an ideal cleanser when the skin cannot tolerate soap in.....**diaper rash seborrheic dermatoses • industrial dermatitis housewives' and infants' eczema • acne vulgaris**

excellent for physicians, dentists and others who wash hands frequently.

send for samples
and try this new **LOWILA cake**

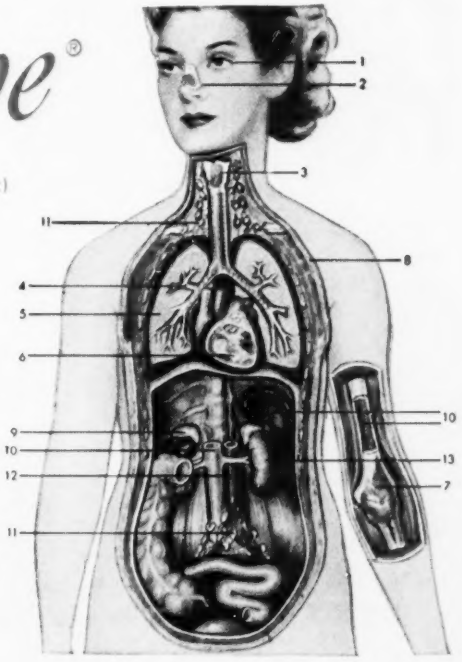
WESTWOOD PHARMACEUTICALS
division of Foster-Milburn Co.
468 Dewitt St., Buffalo 13, N. Y.

When writing for LOWILA samples, please address Dept. D

Cortone®

ACETATE

(CORTISONE ACETATE, MERCK)



The many indications for CORTONE *highlight its therapeutic importance in everyday practice*

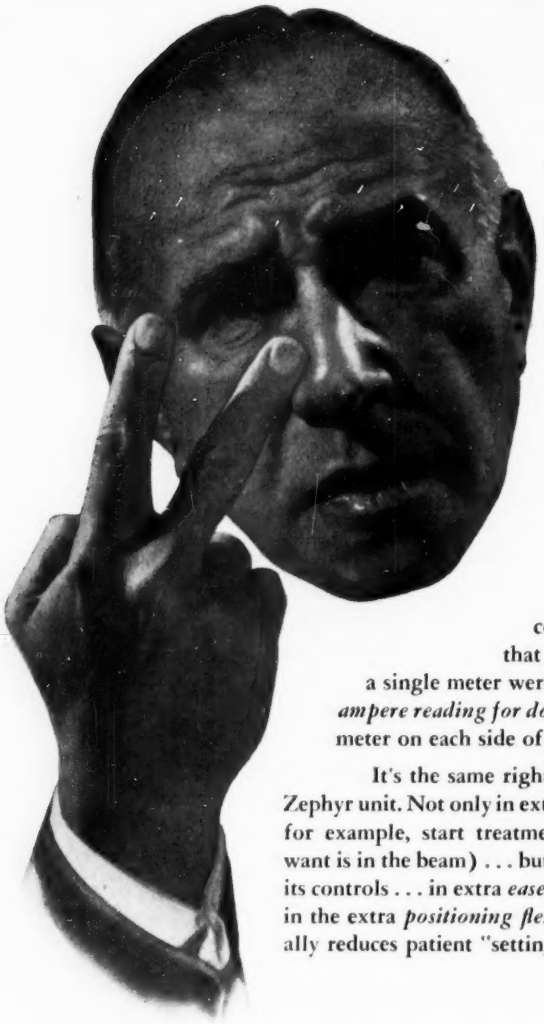
Primary Site of Pathology and Indications

1. EYE—Inflammatory eye disease. **2. NOSE**—Intractable hay fever. **3. LARYNX**—Laryngeal edema (allergic). **4. BRONCHI**—Intractable bronchial asthma. **5. LUNG**—Sarcoidosis. **6. HEART**—Acute rheumatic fever with carditis. **7. BONES AND JOINTS**—Rheumatoid arthritis; Rheumatoid spondylitis; Acute gouty arthritis; Still's Disease; Psoriatic arthritis. **8. SKIN AND CONNECTIVE TISSUE**—Pemphigus; Exfoliative dermatitis; Atopic dermatitis; Disseminated lupus erythematosus; Scleroderma (early); Dermatomyositis; Poison Ivy. **9. ADRENAL GLAND**—Congenital adrenal hyperplasia; Addison's Disease; Adrenalectomy for hypertension, Cushing's Syndrome, and neoplastic diseases. **10. BLOOD, BONE MARROW, AND SPLEEN**—Allergic purpura; Acute leukemia† (lymphocytic or granulocytic); Chronic lymphatic leukemia.† **11. LYMPH NODES**—Lymphosarcoma†; Hodgkin's Disease†. **12. ARTERIES AND CONNECTIVE TISSUE**—Periarteritis nodosa (early). **13. KIDNEY**—Nephrotic Syndrome, without uremia (to induce withdrawal diuresis). **14. VARIOUS TISSUES**—Sarcoidosis; Angioneurotic edema; Drug sensitization; Serum sickness; Waterhouse-Friderichsen Syndrome.

†Transient beneficial effects.

CORTONE *is the registered trade-mark of Merck & Co., Inc. for its brand of cortisone.*

MERCK & CO., INC.
Manufacturing Chemists
RAHWAY, NEW JERSEY

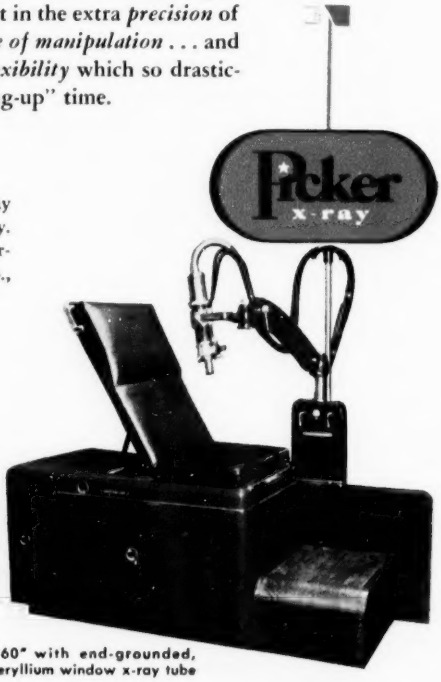


but why two?

Many a doctor has been puzzled to learn that we put *two* milliammeters in every Picker "Zephyr" control instead of the usual one. Puzzled, that is, until he realizes what could happen if a single meter were to fail *when he is depending on milliampere reading for dosage control.* In the "Zephyr", a separate meter on each side of the ma circuit rules out that possibility.

It's the same right down the line at every point, in every Zephyr unit. Not only in extra *safeguards* (you can't, for example, start treatment unless the filter you want is in the beam) . . . but in the extra *precision* of its controls . . . in extra *ease of manipulation* . . . and in the extra *positioning flexibility* which so drastically reduces patient "setting-up" time.

There is a Picker "Zephyr" for any technic you may wish to use in superficial or intermediate x-ray therapy. And one for every therapy work load . . . occasional, intermittent, or continuous heavy-duty. Picker X-ray Corp., 25 So. Broadway, White Plains, N. Y.



"Zephyr"

x-ray therapy units
60 KV
120 KV
140 KV

Zephyr "60" with end-grounded, end-fire beryllium window x-ray tube

A. M. A.
Archives of Dermatology and Syphilology

VOLUME 67 FEBRUARY 1953 NUMBER 2

COPYRIGHT, 1953, BY THE AMERICAN MEDICAL ASSOCIATION

LOCAL OXYTETRACYCLINE ("TERRAMYCIN") THERAPY OF SKIN INFECTIONS

CARROLL S. WRIGHT, M.D.
AND
DONALD N. TSCHAN, M.D.
PHILADELPHIA

THE ANTIBIOTIC known as oxytetracycline ("terramycin") is produced from a species of earth mold (Streptomyces rimosus) and as a crystalline amphoteric substance reacting chemically with certain acids or bases to form stable crystalline salts. In contrast to the accidental discovery of penicillin, by Fleming in 1929, the development of oxytetracycline resulted from an organized concentrated search for a therapeutic agent against bacterial, rickettsial, spirochetal, and certain viral and protozoan organisms. The actual program of collecting 100,000 soil samples from a multitude of locations on the various continents of the world has been described by Kane, Finlay, and Sobin.[1] It was after a prolonged screening process that an actinomycete, S. rimosus (so called because of the cracked appearance of the growth on agar medium), yielded a new antibiotic.[2]

Oxytetracycline was first prepared in pure crystalline form by Regna and Solomons.[3] The antibiotic occurs as a bright yellow powder, soluble in water and common organic solvents. In dilute aqueous solution the hydrochloride salt is very stable; at pH 1.0 to 2.5 there is no detectable loss of activity at 5 C. or at 25 C. for at least 30 days. Samples stored at 5 C. at pH 3.0 to 9.0 show no detectable loss for at least a month. In the dry state, both oxytetracycline and its hydrochloride are remarkably stable for two years.

Livingood,[4] in a study based upon in vitro sensitivity tests and clinical experience, showed that oxytetracycline gave excellent results in the treatment of infections caused by hemolytic staphylococci, streptococci, and miscellaneous Gram-negative organisms but was not superior to other available antibiotics. The effects were questionable in Proteus infections and satisfactory to excellent in a high percentage of Pseudomonas infections.

From the Department of Dermatology, Temple University School of Medicine.

"Terramycin" for this investigation was furnished by Chas. Pfizer & Company, Inc., Brooklyn.

1. Kane, J. H.; Finlay, A. C., and Sobin, B. A.: Antimicrobial Agents from Natural Sources, Ann. New York Acad. Sc. **53**:226-228 (Sept. 15) 1950.

2. Finlay, A. C.; Hobby, G. L.; P'an, S. Y.; Regna, P. P.; Routien, J. B.; Seeley, D. B.; Shull, G. M.; Sobin, B. A.; Solomons, I. A.; Vinson, J. W., and Kane, J. H.: Terramycin: a New Antibiotic, Science **111**:85 (Jan. 27) 1950.

3. Regna, P. P., and Solomons, I. A.: The Chemical and Physical Properties of Terramycin, Ann. New York Acad. Sc. **53**:229-237 (Sept. 15) 1950.

4. Livingood: A. M. A. Arch. Dermat. & Syph., to be published.

There being no previous publications indicating the value of oxytetracycline ointment in the field of dermatology, an intensive study was begun in November, 1950, to determine its therapeutic value when applied locally and also to determine any untoward side-effects. To date, oxytetracycline ointment has been applied locally in the treatment of 845 patients, with a complete follow-up of 635. Of the 635 patients, 391 had various dermatoses and in the remaining 244 oxytetracycline was applied to study its healing effect on wounds following minor skin surgery. In the accompanying table are presented a brief analysis of the results in the dermatoses treated with oxytetracycline ointment and mention of its effect in wound healing.

As expected, the most striking results were observed in the treatment of impetigo contagiosa. The ointment was rubbed in gently but thoroughly every three hours. In not a single case was it necessary to change the therapy.

Analysis of Results of Treatment with Oxytetracycline Ointment

Diagnosis	No. of Patients	No. Cured Within						No. Not Cured
		24 Hr.	48 Hr.	72 Hr.	5 Days	7 Days	14 Days or More	
Impetigo contagiosa	90	2	6	29	27	18	8	0
Folliculitis and sycosis vulgaris	106	1	4	4	10	29	53	5
Impetiginized miscellaneous eruptions (see text)	133	..	1	5	15	39	50	23
Acne vulgaris	17	..	..	..	..	..	..	17
Paronychia	8	..	..	..	..	4	4	..
Kaposi's varicelliform eruption	1	..	..	1	..	..	..	..
Other dermatoses (see text)	36	..	..	..	..	..	..	36
Wound healing (after minor surgery)	244*	..	..	..	..	..	..	..

* Healing was without complication in all cases.

Folliculitis and sycosis vulgaris include everything from a simple superficial involvement of the hair follicles to a deep-seated coccogenous sycosis of the beard. Response to therapy was in direct relation to the depth of the infection, the deep-seated follicular infections requiring a much longer time for a cure or to obtain improvement. Included is one case of severe folliculitis nuchae scleroticans (dermatitis papillaris capillitii) which was remarkably improved but not completely cured at the time this paper was written.

Impetiginized miscellaneous eruptions include secondarily infected contact dermatitis, atopic eczema, dermatophytosis, and seborrheic eczema. The illustrations demonstrate the 72-hour response to oxytetracycline ointment in impetiginized contact dermatitis and in impetiginization following a burn from overexposure to a home sun lamp. No other therapy was used in either case.

Only a small number of patients with acne vulgaris have been treated to date, and these were observed for the effects of oxytetracycline ointment on the pustule count. Three of 17 were much improved, but in the other cases effects were negligible.

To determine whether oxytetracycline applied locally might be beneficial in virus diseases and in eruptions other than infections, a number of patients with dermatoses which are listed in the Table as miscellaneous were given oxytetracycline ointment without other therapy. The diseases included psoriasis, herpes zoster, herpes simplex, verruca vulgaris, seborrheic eczema, molluscum contagio-

Fig. 1.—Impetiginized contact dermatitis. *A*, appearance before application of oxytetracycline ("terramycin") ointment; *B*, appearance 72 hours after beginning of treatment.

Fig. 2.—Impetiginization following overexposure to home sun lamp. *A*, appearance before application of oxytetracycline ("terramycin") ointment; *B*, appearance 72 hours after start of therapy.

sum, and erysipeloid (one case). In not a single one of these conditions was a cure effected. The viral infections of the skin showed no response to therapy other than perhaps a slight soothing effect which could have been brought about by simple petrolatum.

Two hundred forty-four patients were given oxytetracycline ointment to dress wounds following removal of various types of skin growths, such as verrucae, molluscum contagiosum, pyogenic granulomas, nevi, keratoses, and skin cancer. In all but two cases the wounds healed without complication. In these two, use of the ointment was discontinued because of sensitivity to the petrolatum base.

REACTIONS

Of the 635 patients who used oxytetracycline ointment and were followed through completely, only four showed irritation which led to the discontinuance of the medication. Patch tests on these four patients revealed sensitivity to the petrolatum base. All patch tests with oxytetracycline hydrochloride elicited negative reactions.

SUMMARY

A study is presented in which oxytetracycline ("terramycin") ointment was applied topically to 845 patients, 635 of whom were followed through to the completion of therapy.

Impetigo contagiosa responded promptly, 82 of 90 patients being cured within 24 hours to 7 days.

Deeper infections, such as folliculitis and sycoses vulgaris, responded more slowly, but 101 of 106 patients were cured.

Oxytetracycline ointment proved efficacious in clearing up secondary impetiginization in cases of contact dermatitis, atopic eczema, dermatophytosis, and seborrheic eczema.

Viral diseases of the skin and dermatosis other than bacterial infections failed to respond to oxytetracycline applied topically.

In the oxytetracycline treatment of wounds following minor skin surgery, infection did not develop in a single case.

In not a single instance did oxytetracycline hydrochloride cause irritation of the skin. In four cases in which irritations occurred, these were proved by patch testing to be due to the petrolatum base.

1402 Spruce St. (2).

CHROMOBLASTOMYCOSIS

Report of First Case Recognized in Michigan, Apparently Contracted in South Carolina

A. JAMES FRENCH, M.D.
ANN ARBOR, MICH.
AND
SHERWOOD R. RUSSELL, M.D.
ST. JOHNS, MICH.

THE FIRST case of chromoblastomycosis in the United States was reported by Medlar [1] and by Lane,[2] who discussed it from different points of view. This case was found in Massachusetts. A few additional cases from North America have been added to the literature. Reports include one case by Wilson, Hulsey, and Weidman,[3] from Texas, in 1933; one by Martin, Baker, and Conant,[4] from North Carolina, in 1936; one by Moore and Mapother,[5] from Missouri, in 1940; one by Emmons, Hailey, and Hailey,[6] from Georgia, in 1941; one by Weidman and Rosenthal,[7] from Pennsylvania, in 1941; two by Moore, Cooper, and Weiss,[8] from Missouri in 1943; one by Binford, Hess, and Emmons,[9] from Georgia, in 1944, and one by Mundt and Moore,[10] from Louisiana, in 1947-1948.

From the Department of Pathology, University of Michigan, and the Clinton Memorial Hospital, St. Johns, Mich.

1. Medlar, E. M.: A Cutaneous Infection Caused by a New Fungus, Phialophora Verrucosa, with a Study of the Fungus, J. M. Res. **32**:507-521 (July) 1915.

2. Lane, C. G.: A Cutaneous Disease Caused by a New Fungus (Phialophora Verrucosa), J. Cutan. Dis. **33**:840-846 (Dec.) 1915.

3. Wilson, S. J.; Hulsey, S., and Weidman, F. D.: Chromoblastomycosis in Texas, Arch. Dermat. & Syph. **27**:107-122 (Jan.) 1933.

4. Martin, D. S.; Baker, R. D., and Conant, N. F.: A Case of Verrucous Dermatitis Caused by Hormodendrum Pedrosoi (Chromoblastomycosis) in North Carolina, Am. J. Trop. Med. **16**:593-619 (Sept.) 1936.

5. Moore, M., and Mapother, P.: Chromomycosis of the Face: Report of a Case and a Study of the Causative Organism, Phialophora Verrucosa, Arch. Dermat. & Syph. **41**:42-54 (Jan.) 1940.

6. Emmons, C. W.; Hailey, H., and Hailey, H.: Chromoblastomycosis: Report of the Sixth Case from Continental United States, J. A. M. A. **116**:25-28 (Jan. 4) 1941.

7. Weidman, F. D., and Rosenthal, L. H.: Chromoblastomycosis: A New and Important Blastomycosis in North America, Arch. Dermat. & Syph. **43**:62-84 (Jan.) 1941.

8. Moore, M.; Cooper, Z. K., and Weiss, R. S.: Chromomycosis (Chromoblastomycosis): Report of 2 Cases, J. A. M. A. **122**:1237-1243 (Aug. 28) 1943.

9. Binford, C. H.; Hess, G., and Emmons, C. W.: Chromoblastomycosis: Report of a Case from Continental United States and Discussion of the Classification of the Causative Fungus, Arch. Dermat. & Syph. **49**:398-402 (June) 1944.

10. Mundt, L. K., and Moore, M.: Chromomycosis: Report of a Case from Louisiana with a Discussion of Its Clinical and Mycologic Features, New Orleans M. & S. J. **100**:558-565 (June) 1948.

Weidman and Rosenthal [7] in 1941 summarized 110 cases of chromoblastomycosis from the literature. The majority were reported in the West Indies, Central and South America, Africa, the East Indies, Burma, and Japan. Most of the patients were 30 to 50 years of age, and 102 of the 110 were male. These authors noted that chromoblastomycosis often followed an injury to skin by wood, as in the case reported here. Martin [11] confirmed this finding in a report in which strains of Phialophora isolated from wood by Kress were antigenically identical with those isolated from patients with chromoblastomycosis. Emmons [12] reported the isolation of fungi, pathogenic for man, from soil, as have many others, but did not refer to chromoblastomycosis, although some reports in the literature suggested that contaminated soil might have been the source of infection.

The terminology of the condition is somewhat unsatisfactory in that the term chromoblastomycosis, or chromomycosis, suggests that the lesions as seen clinically have an unusual color, but actually this is not the case. However, the organisms are brown both in unstained sections and in tissue sections stained with hematoxylin and eosin. They are brownish black on culture media. Unlike blastomycetes, they reproduce by splitting and not by budding; blastospores (buds) are not produced in tissues or in cultures. Since dermatitis verrucosa is entirely a nonspecific term, the designation of chromoblastomycosis assigned to this disease by Pedroso and Gomez [13] is retained in most reports that have appeared in the literature. Pedroso is said to have described the first case in Brazil in 1911 and to have designated the disease black blastomycosis.

Three species of fungi isolated from patients with chromoblastomycosis are Phialophora verrucosa (Thaxter, 1915), Hormodendrum (or Fronseceae) pedrosoi (Brumpt, 1922) and Hormodendrum (or Fronseceae) compactum (Carrión, 1935 [14]). Carrión,[15] Carrión and Emmons,[16] and Binford, Hess, and Emmons [9] have discussed the classification of these fungi. H. pedrosoi and H. compactum each produces antibody against the other, but P. verrucosa does not produce cross agglutination with the other two. The strains of fungi isolated from cases of chromoblastomycosis elicit antibody formation when injected in rabbits and can be distinguished serologically and morphologically in cultures but not in tissue sections, according to Conant and Martin.[17] (The papers to which reference has been made should be consulted for mycologic and cultural details and for suggested nomenclature.)

11. Martin, D. S.: The Antigenic Similarity of a Fungus Cadophora Americana Isolated from Wood Pulp to Phialophora Verrucosa Isolated from Patients with Dermatitis Verrucosa (Chromoblastomycosis), Am. J. Trop. Med. **18**:421-426 (July) 1938.

12. Emmons, C. W.: The Isolation from Soil of Fungi Which Cause Disease in Man, Tr. New York Acad. Sc. **14**:51-54 (Nov.) 1951.

13. Pedroso, A., and Gomez, J. M.: Quatro casos de dermatite verrucosa produzida pela Phialophora Verrucosa, Bol. Soc. med.-cirurg. mil. **5**:263-265, 1919-1920.

14. Carrión, A. L.: Chromoblastomycosis: Preliminary Report of a New Clinical Type of the Disease Caused by Hormodendrum Compactum, Nov. Sp., Puerto Rico J. Pub. Health **10**:543-548 (June) 1935.

15. Carrión, A. L.: The Specific Fungi of Chromoblastomycosis, Puerto Rico J. Pub. Health **15**:340-361 (June) 1940; Chromoblastomycosis, Mycologia **34**:424-441 (July-Aug.) 1942.

16. Carrión, A. L., and Emmons, C. W.: A Spore Form Common to 3 Etiologic Agents of Chromoblastomycosis, Puerto Rico J. Pub. Health **11**:114-115 (Sept.) 1935.

17. Conant, N. F., and Martin, D. S.: The Morphologic and Serologic Relationships of the Various Fungi Causing Dermatitis Verrucosa (Chromoblastomycosis), Am. J. Trop. Med. **17**:553-577 (July) 1937.

The lesions, according to Ash and Spitz,[18] usually occur on the exposed parts, particularly the extremities and the head, but almost all parts of the body have been noted to be involved. Conant, Martin, Smith, Baker, and Callaway [19] stated that in all the reported cases except two the lesions were localized to a single skin area or extremity. No visceral involvement, other than questionable regional metastases in one or two instances, had been reported. In an advanced stage the disease may be incurable, save by amputation.

The lesion begins as a small papule and extends eccentrically like an area of ringworm. In early stages the area is limited and is red or violaceous, and the margin is indurated. Crops of new lesions tend to occur along lymphatics. A variety of clinical forms of the disease may occur, as indicated by Pardo-Castello, Rio Leon, and Trespalacios [20]: (1) verrucous, (2) tuberculoid, (3) syphiloid, (4) psoriasiform, and (5) cicatricial and elephantiasic. The verrucous form of the lesion is the

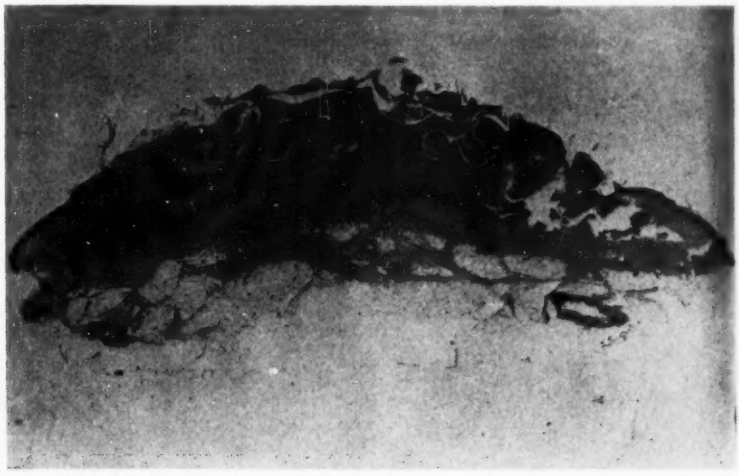


Fig. 1.—Section of the gross lesion, 4482-LBD, a papillomatous verrucous granuloma in the skin. Hematoxylin and eosin stain; × 6.

common one, and the involved area may protrude 1 to 2 mm. above the normal skin, with a central portion which is cauliflower-like. Pedunculation, secondary infection, and ulceration may occur, but the lesion tends to remain dry. If allowed to progress untreated, the lesion may involve an entire extremity within a period of 4 to 15 years. Spontaneous healing may occur. Most of the lesions are painless unless ulcerated, and, while pruritus is not a common symptom, Carrión [14] reported severe itching in his cases from Puerto Rico.

18. Ash, J. E., and Spitz, S.: Pathology of Tropical Diseases, Philadelphia and London, W. B. Saunders Company, 1945, p. 153.

19. Conant, N. F.; Martin, D. S.; Smith, D. T.; Baker, R. D., and Callaway, J. L.: Manual of Clinical Mycology, Military Medical Manuals, National Research Council, Philadelphia, W. B. Saunders Company, 1947, pp. 94-109.

20. Pardo-Castello, V.; Rio Leon, E., and Trespalacios, F.: Chromoblastomycosis in Cuba, Arch. Dermat. & Syph. **45**: 19-32 (Jan.) 1942.

Direct smears made from crusts of the lesions, cleared in a drop of 10% potassium hydroxide solution on a glass slide, will reveal the brownish organisms. They also are identified easily in tissue sections stained by routine hematoxylin and eosin techniques. The organisms appear as single or grouped round brown bodies, which divide by splitting and do not bud. The single organism is 6 to 12 μ in diameter. Division by splitting may result in groups of rounded septate forms.

Microscopically, the papillomatous lesion (Fig. 1) is seen to be hyperkeratotic, but less so than in North American blastomycosis, and keratin cysts are prominent. The granulation tissue, which may replace the full thickness of the dermis or be limited to the upper portions of the corium, contains purulent and suppurative foci. Mononuclear cells are present in addition to the polymorphonuclear leucocytes. Plasma cells, Russell-Plimmer fuchsinophile bodies, lymphocytes, mononucleated

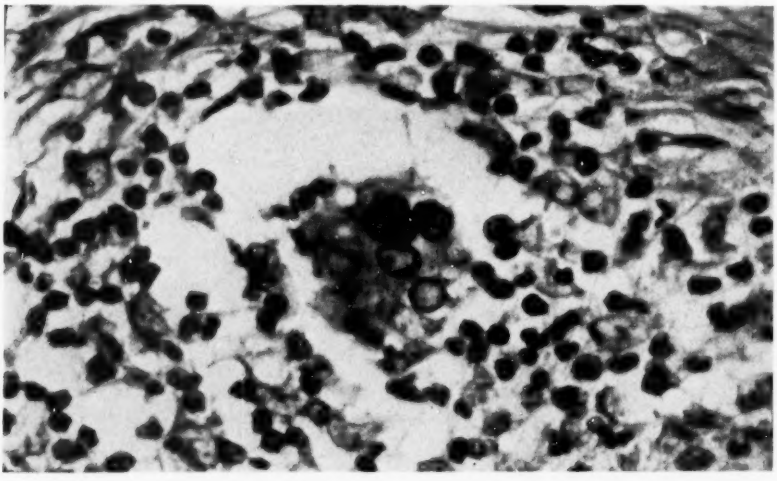


Fig. 2.—Fungal bodies in a giant cell; single bodies and groups showing the septate division. Inflammatory response at the margins of the giant cell includes polymorphonuclear leukocytes, lymphocytes, plasma cells, mononuclear phagocytes, and fibroblasts. Giemsa stain; × 330.

and multinucleated phagocytes, and giant cells (Fig. 2) are numerous. Fibroblasts, angioblasts, and delicate, new-formed blood vessels with prominent endothelial cells are present in the granulation tissue.

The organisms (Figs. 2, 3, and 4) are found in the purulent and suppurative foci and are single or multiple brown bodies 6 to 12 μ in diameter. Most of the fungal cells are free in the exudate, but a few may be phagocytosed by multinucleated giant cells.

Toluidine blue, Schiff (Fig. 3), Giemsa (Fig. 2), and Best-Bodian stains were utilized, and all were more precise than the routine hematoxylin and eosin (Fig. 4) technique, but they masked the natural brown color of the organism and added nothing to ease of diagnosis.

The patient referred to in this report was a 74-year-old white man, native of Michigan, who visited in South Carolina in 1950. He had had a "sliver" of wood in the skin of the

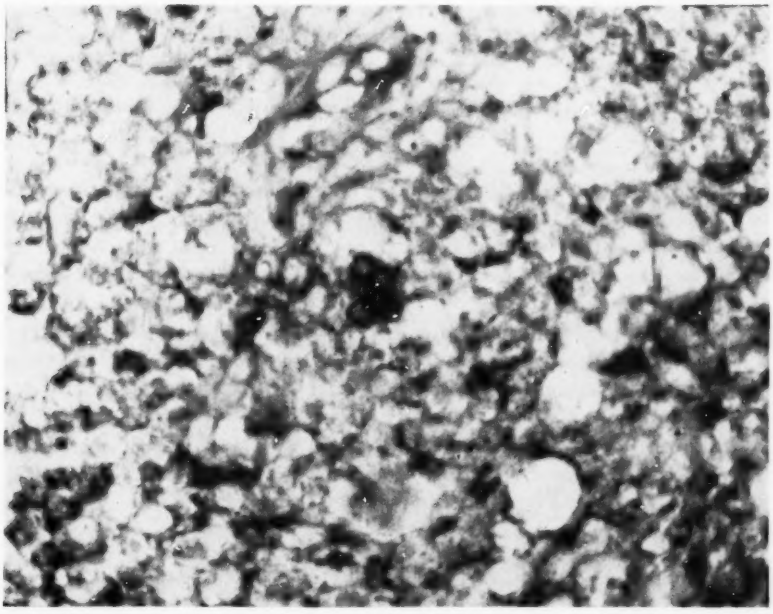


Fig. 3.—Septate division of the fungus. Amorphous background is attributable to the staining technique. Schiff stain; × 330.

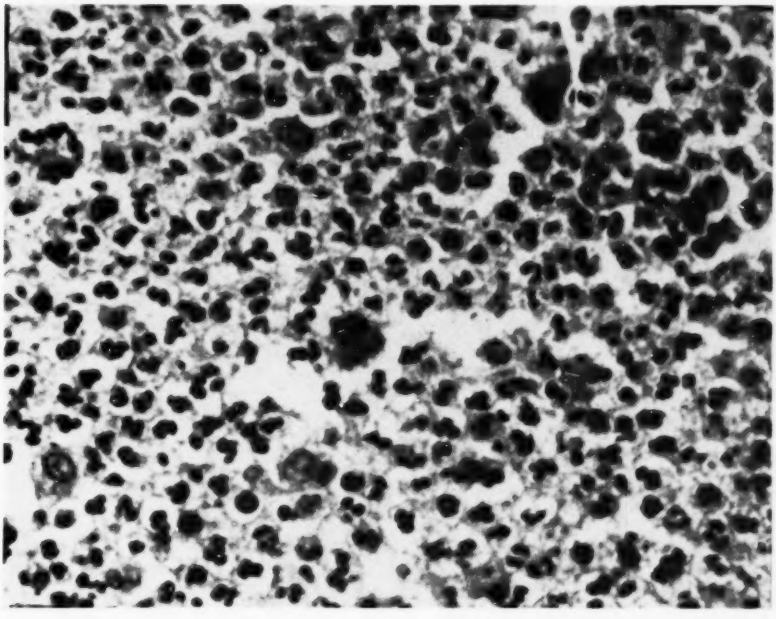


Fig. 4.—Septate division of the fungus; purulent exudate and mononuclear phagocytes in the dermis. Hematoxylin and eosin stain; × 330.

dorsum of the left wrist at that time. The wound healed, but it reopened spontaneously in October, 1951, and enlarged until the entire verrucous lesion (4482-LBD) was excised in December, 1951. A culture was not obtained. Examination of the patient in January, 1952, indicated that the entire lesion had been excised, and no recurrence was found. Gross and microscopic characteristics were typical and have been described in the general discussion of the lesions.

SUMMARY

This is thought to be the first case of chromoblastomycosis reported from Michigan, but apparently the disease was contracted in South Carolina. The condition is a specific chronic infective granuloma, usually caused by one of three related fungi: Phialophora verrucosa, Hormodendrum (or Fronseceae) pedrosoi, or Hormodendrum (or Fronseceae) compactum. Serologically, and by morphologic cultural characteristics, these fungi can be distinguished. The disease is limited to the skin, and visceral involvement has not been reported. The course is prolonged unless the disease is treated. Complete early local excision may be curative.

The patient was injured with wood. This association has been noted in other reported cases of chromoblastomycosis.

In microscopic sections granulation tissue is present in and beneath the epidermal papillae and consists of purulent foci, multinucleated foreign body or Langhans' type giant cells, plasma cells, Russell-Plimmer fuchsinophile bodies, mononuclear phagocytes, and lymphocytes. Hyperkeratosis and papillomatous overgrowth of the epidermis are less striking than in North American blastomycosis and less tuberculoid than in coccidioidal mycosis. The fungal bodies are round or septate, are brown in sections stained with hematoxylin and eosin, 6 to 12 μ in diameter, and occur in the purulent foci or, less commonly, in the giant cells.

NODULAR VASCULITIS

Report of Two Cases Associated with Hypertension

S. IRGANG, M.D.
NEW YORK

IT IS only within recent years that nodular vasculitis has become recognized and has attained prominence as a definite disease entity despite opinions to the contrary.[1] This has been accomplished largely through the investigations of Montgomery and O'Leary and their associates,[2] who were the first to describe this disease in the American literature. Toward the end of the nineteenth century and in the early years of this century cases of nodular vasculitis were, as they still are, called nontuberculous types of erythema induratum. Audry was probably the first to report a case of the nontuberculous form of erythema induratum.[3] His patient was a woman aged 34, who had a recurrent symmetrical superficial and deep-seated nodular eruption on the legs and feet. These lesions, present for five years, were slightly tender and painful, and several became necrotic and ulcerated. Galloway,[4] Philippson,[5] and Whitfield[6] described similar cases, but it was Whitfield who stressed the occurrence of this disease in women after the age of 30 and particularly in those in early middle life. Recently, Bettley[1b] reported a case of nodular vasculitis under the designation of nontuberculous type of erythema induratum. His patient was a woman aged 50, with lesions on the upper and lower extremities and on the buttocks. Forman[7] presented a case of nodular vasculitis under the title of lipophagous granuloma. His patient was a woman aged 50, with a recurrent nodular

From the Department of Dermatology and Syphilology of the Harlem Hospital, Dr. Alexander Altschul, Medical Director.

1. (*a*) Anderson, C. R.: Nodular Vascular Disease of the Legs, Correspondence, J. A. M. A. **128**:1249 (Aug. 25) 1945. (*b*) Bettley, F. R.: Erythema Induratum (Whitfield), Proc. Roy. Soc. Med. **43**:391 (May) 1950.

2. Montgomery, H.; O'Leary, P. A., and Barker, N. W.: Nodular Vascular Diseases of the Legs: Erythema Induratum and Allied Conditions, Collect. Papers Mayo Clin. **36**:461, 1944; J. A. M. A. **128**:335 (June 2) 1945.

3. Audry, C.: Étude de la lésion de l'érythème induré (de Bazin) sur la notion du lymphatisme, Ann. dermat. et syph. **29**:209, 1898.

4. Galloway, J.: Erythema Induratum, Clin. J. **13**:184, 1898-1899.

5. Philippson, L.: Über Phlebitis nodularis necrotisans (Beitrag zu dem Studium der Tuberculides von Darier), Arch. Dermat. u. Syph. **55**:215, 1901.

6. Whitfield, A.: On the Nature of the Disease Known as Erythema Induratum Scrofulosorum, Brit. J. Dermat. **13**:386 (Oct.) 1901; A Further Contribution to Our Knowledge of Erythema Induratum, ibid. **17**:241 (July) 1905; On Inflammatory Nodules of the Hypoderm, ibid. **21**:1 (Jan.) 1909.

7. Forman, L.: Lipophagous Granuloma (Telford), Brit. J. Dermat. **50**:558 (Oct.) 1938.

eruption of 20 months' duration on the lower extremities. In Pick's [8] two patients with so-called persistent forms of erythema nodosum these could have been examples of nodular vasculitis; his patients were young women aged 17 and 19, respectively.

O'Leary and his associates [9] were the first to direct attention to the coexistence of hypertension in these patients. Their patient was a woman aged 54, with sys-

Fig. 1.—The lesions, limited to the lower extremities, are scarcely elevated above the surface.

tolic blood pressure ranging from 190 to 230 mm. Hg and diastolic 120 mm. Hg. Bettley's patient had a blood pressure of 140/90. During the past few years I had the opportunity to observe two cases of nodular vasculitis associated with hypertension. Both patients were Negro women, one in the fifth and the other in the sixth decade of life. These cases were considered of sufficient interest to record.

8. Pick, W.: Über die persistierende Form des Erythema nodosum, Arch. Dermat. u. Syph. **72**:361, 1904.

9. O'Leary, P. A.; Montgomery, H., and Brunsting, L. A.: Cases for Diagnosis, Arch. Dermat. & Syph. **50**:212 (Sept.) 1944.

REPORT OF CASES

CASE 1.—H. S., a Negro woman, aged 57, presented an eruption on the legs and on the right foot of 14 months' duration. The lesions were most numerous on the posterior aspect of the legs. The eruption consisted of deep-seated firm, flat, coin-sized nodules, which were usually ill-defined and flesh-colored, pinkish red, or brownish black, and some of which were adherent to the overlying skin. At their inception the nodules, which originated in the subcutaneous tissues, were

Fig. 2.—Low-power photomicrograph of the subcutis, showing thickened vascular walls with narrowed lumina, diffuse fibrosis, and foci of panniculitis. Hematoxylin and eosin stain.

flesh-colored, tender, and painful. Those lesions which extended upward to involve the superficial layers of the skin were scarcely elevated above the surface. Ulceration did not occur. The lesions healed spontaneously after several months, but they continued to recur. Resolved lesions left either no trace or different shades of brownish pigmentation, depending on the depth of the preceding lesion; those which remained confined to the subcutaneous tissues left no residual pigmentation. A few coin-sized, firm, brownish black flat nodules were noted on the dorsal and lateral aspects of the right foot. Pitting edema was detected over both ankles.

In addition to the cutaneous lesions, the patient complained of intermittent attacks of throbbing headache and dizziness for the past 15 months. The blood pressure was 200/100. Serologic tests of the blood for syphilis were reported as negative. A urinalysis showed normal values. An intracutaneous injection of 0.01 cc. of old tuberculin in dilution of 1:10,000 produced a moderately positive local reaction. A hemogram was normal except for a neutropenia (42%) and a lymphocytosis (46%). An electrocardiogram showed evidences of left ventricular hypertrophy, and a roentgenogram of the chest showed left ventricular enlargement of the heart and sclerosis of the aorta.

Fig. 3.—Medium-power photomicrograph of the subcutis shown in Figure 2. Note the relationship of the cellular infiltrates to the smaller blood vessels. Hematoxylin and eosin stain.

Histologic examination of a pinkish red cutaneous nodule showed pathologic changes throughout the skin, but the most profound alterations were noted in the subcutis. Here the larger blood vessels showed decided thickening of their walls and narrowing of their lumina. The walls of most of the smaller blood vessels were also thickened but to a much less degree. Thromboses were not observed. The reaction of the lining endothelial cells was minimal, being

characterized by slight swelling and occasionally by some proliferation. Fibrosis was extensive, and connective tissue replacement of fat was striking. There were patchy areas of fat necrosis. The dense perivascular cellular infiltrates were not large, and they were confined to the smaller vessels. They consisted of lymphocytes and fewer, though prominent, plasma cells; in some foci the plasma cells outnumbered the lymphocytes. An occasional epithelioid cell was also noted. Giant cells were absent.

The walls of most of the blood vessels in the cutis were slighty thickened. Some were mildly dilated and a few showed slight swelling and, at times, proliferation of their lining endothelial cells. A thinly scattered fibrosis was likewise noted in this layer, but perivascular cellular infiltrates were lacking.

The epidermis was irregular. Some regions showed narrowing of the suprapapillary rete with blunting or absence of rete pegs, while in other areas rete peg proliferation was noted. The stratum granulosum was uniformly narrowed, but there was slight hyperkeratosis.

CASE 2.—R. H., a Negro woman, aged 41, had an eruption on the legs for more than one year, although the exact duration was unknown. The eruption consisted of firm, slightly painful and tender, ill-defined flat nodules, of bean to hazelnut size, flesh-colored or pinkish red, and scarcely elevated above the surface. They were most numerous on the anterior aspect of the lower half of the legs. The deep-seated lesions showed no visible inflammatory aspect, but as the process approached the surface they assumed a pinkish red color. The lesions did not ulcerate. They usually healed spontaneously within three or four months, but on occasion persisted as long as nine months. Recurrences were common. The deep-seated nodules healed without leaving a trace, but those which involved the more superficial layers of the skin left pigmentary residua at sites of resolution. Pretibial edema was observed bilaterally.

The patient also complained of severe intermittent headaches for the past two years and for the past four years she could not continue at her occupation as a domestic because she tired easily. The blood pressure was 190/110. The blood cholesterol was 200 mg. per 100 cc. The serologic tests of the blood for syphilis were negative. A urinalysis showed normal values. An intracutaneous injection of 0.01 cc. of old tuberculin in dilution of 1:10,000 elicited a weakly positive local reaction. A hemogram was normal except for a neutropenia (54%) and a lymphocytosis (42%). An electrocardiogram showed left ventricular preponderance. A roentgenogram of the chest showed dilatation of the aortic arch and enlargement of the cardiac shadow to the right and left, suggesting hypertensive heart disease.

Histologic examination of a pinkish red cutaneous nodule showed pathologic features almost identical with those observed in Case 1, except that the walls of the blood vessels in the subcutis were not quite so thick and the perivascular cellular infiltrates in this layer were extremely sparse and consisted solely of lymphocytes.

The symptoms and laboratory findings common to both patients were headache, edema of the lower extremities, aortic sclerosis, and neutropenia and lymphocytosis. As a matter of record, the tuberculin tests were positive, but roentgenographic examination of the chest and histologic study of cutaneous lesions in both cases failed to show any evidence of tuberculous disease.

COMMENT

In my experience, nodular vasculitis is a rare disease in the Caucasian race, and this is applicable to the Negro as well. It is only within recent years that this disease has become established as a definite disease entity. This has been attained largely through the investigations of Montgomery and O'Leary, who were probably the first to evaluate comprehensively the clinical and histopathologic features of this disease. Nodular vasculitis is observed chiefly in women in middle life or beyond, and it is commonly associated with hypertension.[10] In Case 1 of my series

10 O'Leary, P. A.; Montgomery, H.; Brunsting, L. A., and Kierland, R. R.: Erythema Induratum with Untoward Reactions from Paraaminosalicylic Acid, Arch. Dermat. & Syph. **62**:606 (Oct.) 1950.

the blood pressure was 200/100, while in Case 2 it was 190/110. Both patients exhibited subjective symptoms referable to the hypertensive state. They also showed roentgenographic evidences of aortic sclerosis, and hematologic study revealed, incidentally, a neutropenia and a lymphocytosis. In view of the age group in which this disease usually occurs, the hypertension may be merely a concomitant finding. Nevertheless, the striking vascular abnormalities in the cutaneous lesions suggests the possibility that they may represent local manifestations of generalized vascular disease.

Despite a definite clinical pattern for nodular vasculitis, it is quite evident that a diagnosis cannot be made without histologic study. For this purpose a pinkish red cutaneous lesion should be excised. The principal pathologic changes are noted in the subcutis, but similar findings on a smaller scale will probably be seen in the cutis. In the subcutis the majority of the vascular walls are thickened and their lumina are narrowed. This results in an inadequate blood supply, which causes the fat necrosis and fibrosis.[11] A milder form of fibrosis will be seen in the cutis if the blood vessels here are affected similarly. I believe it is important to emphasize that the combination of histopathologic findings in the subcutis (vascular abnormalities affecting a majority of blood vessels, diffuse fibrosis, and patchy areas of fat necrosis) favor a diagnosis of nodular vasculitis. Regarding the types of infiltrating cells, epithelioid cells, foreign body giant cells, and plasma cells have been observed regularly in nodular vasculitis.[9] Giant cells were not observed in my sections. Furthermore, in my cases the perivascular cellular infiltrates in the subcutis were present only in relation to the smaller blood vessels. In sections in Case 2 these infiltrates were extremely sparse and they consisted solely of lymphocytes. In neither case were perivascular cellular infiltrates found in the cutis.

SUMMARY

Two cases of nodular vasculitis are presented. In both the disease was associated with hypertension. It occurred in Negro women, one of whom was in the fifth and the other in the sixth decade of life.

Roentgenographic examination showed evidences of aortic sclerosis, and hematologic study disclosed a neutropenia and a lymphocytosis in both cases.

The histopathologic findings in nodular vasculitis are discussed.

11. Abrikossoff, A.: Über die spontan auftretende Fettgewebsnekrose und Fettgranulome, Centralbl. allg. Path. u. path. Anat. **38**:542 (Nov. 15) 1926. Telford, E. D.: Lesions of the Skin and Subcutaneous Tissue in Diseases of the Peripheral Circulation, Arch. Dermat. & Syph. **36**:952 (Nov.) 1937.

PREGNENOLONE ACETATE IN TREATMENT OF MYCETOMA (NOCARDIOSIS)

JOHN H. LAMB, M.D.
FLORENE C. KELLY, Ph.D.
PAUL O. SHACKELFORD, M.D.
GERBERT REBELL
AND
ROLLIN C. KOONS, B.S.
OKLAHOMA CITY

THE PURPOSES of this presentation are (1) to report a case of mycetoma (nocardiosis) in a child who had failed to respond to all the standard forms of therapy and who apparently has been cured by treatment with pregnenolone acetate and (2) to call attention to pregnenolone acetate as an agent free from undesirable metabolic or toxic effects, which has useful antifungal properties that warrant further clinical investigation.

BACKGROUND

With the increased interest in antifungal medicaments, many new approaches are under investigation. The Streptomyces group of Actinomycetes have yielded many new antibiotics which show some antifungal properties, such as acti-dione,® from Streptomyces griseus. Other Streptomycetes may yield less toxic and more potent fungicides. The ideal antifungal drug would be one which could be used both locally and orally, which would diffuse through sweat, the nail bases, and the sebum of the hair follicles and which would thus attack the fungus from within as well as without, with no toxicity to the host. Some reports are already in the literature on the toxicity of certain new antifungal drugs used topically in young children.

Our studies indicate, however, that there are certain steroids with little if any metabolic effect, even in children, which show some antifungal properties. Reiss,[1] Dobes,[2] and others have reported the in vitro and in vivo inhibitory effect of vari-

This paper is Publication No. 22 from the Oklahoma Medical Research Institute and Hospital.

From the Departments of Bacteriology and Dermatology of the University of Oklahoma School of Medicine, and the Oklahoma Medical Research Institute and Hospital.

This study was supported in part by a grant to the Oklahoma Medical Research Institute and Hospital from the Chemical Specialties Co., Inc., of New York. The pregnenolone acetate was supplied by this company.

1. Reiss, F. S.: Steroid Hormones: Their Fungistatic and Genestatic Effect on Pathogenic Fungi, Arch. Dermat. & Syph. **59**:405-415 (April) 1949.

2. Dobes, W. L.: Treatment of Tinea Capitis with Estrogenic Hormones, Arch. Dermat. & Syph. **62**:58-65 (July) 1950.

ous steroid hormones, including testosterone and estrogen, on certain dermatophytes and other pathogenic fungi. Stilbamidine (4,4′-stilbenedicarboxamidine), a stilbene which is related to stilbestrol, has exhibited curative properties in generalized blastomycosis.[3] Curtis and others [4] have shown that diethylstilbestrol, as well as "stilbamidine," was curative in cases of blastomycosis.

These systemically active hormones are not practical for use against chronic mycotic infections in children. In the adult female there is the danger of interrupting the menstrual cycle with the estrogens and of developing hirsutism with testosterone. In the adult male there is the danger of suppressing spermatogenesis with testosterone and of developing feminizing symptoms with the estrogens.

Pregnenolone acetate, a steroid compound that has been used in arthritis, has been shown by numerous investigators [5] to have little metabolic effects in large dosage. For this reason, it was employed in treating a child with mycetoma (nocardiosis) who had failed to respond to all the standard modes of therapy. The dramatic results have prompted us to make this report.

REPORT OF A CASE

History.—J. A. G., a white girl 6 years of age, was first seen on Feb. 20, 1951. On July 15, 1950, she had accidentally stuck a pitchfork into her foot, penetrating the dorsal aspect of the astragalus bone. There immediately appeared a rather superficial infection in the area of trauma, which did not heal rapidly. On July 20 the infected area was incised and drained. The patient was given injections of 300,000 units of penicillin daily for 20 days. The area closed promptly and remained healed until October. At that time a large reddened tumor developed at the site of the old wound. Another incision was performed, and drainage was maintained. Granulation tissue became profuse. Since that time the drainage had been intermittent until the child was first seen by us, and the pain on walking was severe.

Physical Examination.—On initial examination there was noted a marked cicatrization of an area measuring 2 by 3 cm. on the dorsum of the left foot, with two small draining sinuses. There was a full range of motion, but pain was easily elicited. There was good muscle tone in the leg muscles. No lymphadenopathy was present in the left inguinal area. The patient's general condition was poor. There was a definite cachectic appearance, with paleness, anorexia, and loss of weight.

Clinical Laboratory Data.—On March 29, the hemoglobin was 75%; the red blood cell count was 3,870,000, and the white blood cell count 5,300, with 49% neutrophiles, 44% lymphocytes, and 7% monocytes. X-ray examination was made on Feb. 19. Anteroposterior and lateral films of the left foot revealed no evidence of bone or joint changes. Results of urinalysis were normal.

Clinical Course and Treatment.—On Feb. 20, therapy with filtered x-rays with a half-value layer of 1.0 mm. Cu, was started to the involved area of the left foot, with the following factors: 200 kv., 20 ma., skin-target distance, 50 cm., 4 cm. square field, Thoreu A filter, 15 r per minute. Two hundred roentgen units was given every other day, for a total of 1,600 r to the same area. Acet-dia-mer-sulfonamides ("tricombisul," triple sulfonamides), one 1.5 gm. tablet daily, and saturated potassium iodide solution, starting with 3 drops three times a day in a small amount of water (after each meal) and gradually increasing the dose, were also prescribed. Local dressings with a paste of sulfanilamide powder and glycerin were also applied. By March 22, there was some improvement. However, by March 29, there was a new erythematous discrete tumor

3. Schoenbach, E. B.; Miller, J. M.; Ginsberg, M., and Long, P. H.: Systemic Blastomycoses Treated with Stilbamidine, J. A. M. A. **146**:1317-1318 (Aug. 4) 1951.

4. Curtis, A. C., and Harrell, E. R.: The Use of 2 Stilbene Derivatives (Diethylstilbestrol and Stilbamidine) in the Treatment of Blastomycosis, read before the American Dermatological Association, Colorado Springs, April 24, 1952, to be published.

5. White, A., Editor: Symposium on Steroids in Experimental and Clinical Practice, Philadelphia, The Blakiston Company, 1951.

mass above the left ankle on the medial surface 3 by 4 cm. in size. This was tender to touch. At that time the patient was taking 28 drops of saturated solution of potassium iodide three times a day and 1 tablet of acet-dia-mer-sulfonamides daily. The latter dosage was increased to 1 tablet three times a day, and the patient was given oral aluminum penicillin tablets, 25,000 units, 2 tablets four times a day. By April 6 there was little change in the lesion, and on April 13 a course of filtered x-ray therapy over the same area was again started; 150 r was given daily for a total of 750 r additional. In addition, 600,000 units of penicillin procaine was given daily on five successive days, making a total of 3,000,000 units, and 150 mg. aureomycin capsules were administered three times a day.

The reaction to a tuberculin patch test applied on May 4 was negative at the end of 96 hours. At this time, pregnenolone acetate tablets (100 mg. twice daily) were prescribed. All other medication and irradiation were discontinued. The patient was observed regularly. On June 7 the lesion appeared to be somewhat improved and was healing. There was more drainage and a little increased tenderness. By June 27 there was definite healing of the lesion, and at that time the dose of pregnenolone acetate was increased to 300 mg. daily. On July 11, the anterior lesion on the dorsum of the left foot was completely closed, and the one on the medial surface of the ankle was beginning to fill in much better. On August 14, because of a slight 4 mm. ulceration at the old sinus orifice she was given 3% pregnenolone acetate in an oxycholesterol-petrolatum ointment base (aquaphor®) for local use, in addition to the oral therapy. On Nov. 30 the lesion was completely healed, and the medication was decreased to one 100 mg. tablet of pregnenolone acetate daily.

This dosage was continued until Jan. 5, 1952, at which time it was reduced to 100 mg. every other day. The patient had gained 18 lb. (8.2 kg.), and her general health was excellent. There were no signs or symptoms of any metabolic alteration in the patient and no toxic reaction after eight months of continual therapy with pregnenolone acetate. The total dose was approximately 60 gm. When last examined, on June 20, 1952, the patient had been entirely well for six months.

LABORATORY INVESTIGATIONS OF THE ORGANISM

Mycologic Studies.—Microscopic examination of the serum and pus failed to reveal any "sulfur" or soft granules in wet preparations, but on two occasions fixed stained smears revealed a Gram-positive mycelium about 1 μ in diameter, similar in size to Nocardia, with regular swellings and contractions suggestive of fragmentation. The pus was inoculated Feb. 20, 1951, on Sabouraud's dextrose agar at 22 C. and blood agar (5% human blood) at 37 C. No growth was noted on either medium. On April 23, more cultures were made on blood agar base (difco®) and Sabouraud's dextrose agar. All the cultures were incubated at 22 C. After 10 days a smooth white creamy convoluted growth appeared on two tubes of blood agar base.

Cellular Morphology: On primary isolation the organism cultured from the lesion was an aerobic, strongly acid-fast, long, slender bacillus-like form in which no branching was evident. It was refractory to staining by Gram's method, the majority of the cells coloring poorly, unevenly, or not at all. Cells which did stain were Gram-positive. The bacilli or short filaments frequently appeared to be vacuolated and enclosed in a refractive wall. The intensity of the acid-fast reaction diminished in subcultures. Occasional rudimentary branching of the bacilli was observed in unstained preparations of one- to two-day-old broth cultures under the phase microscope. Definite branching was seen in stained impression films made of microscopic colonies on agar plate cultures which had been incubated at 37 C. for 15 hours.

Cultural Properties: Growth in a variety of broth and agar plate cultures was visible in 24 to 48 hours. The organism developed a 3 mm. smooth creamy-white raised colony on Sabouraud's medium incubated at room temperature and also on blood agar held at 37 C., on which it was nonhemolytic. A decided contrast to this

smooth type of colony was the growth which developed on nutrient agar and on dextrose agar at 37 C. Here the colony was flat, rough, and of light buff color, like fine sandpaper. Prolonged incubation did not cause increased pigmentation or the heaped-up crumbly roughness of typical Nocardia asteroides colonies. Broth cultures were clear, with a finely granular pellicle or sediment, according to the medium and age of the culture. Cultures of the organism proved to be inactive biochemically in a number of tests: Dextrose, sucrose, lactose, and maltose were not fermented; gelatin was not liquefied; neither hydrogen sulfide nor indole was produced. Litmus milk became slightly alkaline. Paraffin was utilized as the sole source of carbon.

Pathogenicity: Of four guinea pigs, each inoculated intraperitoneally with 0.5 mg. saline or saline-mucin suspensions of the fungus, three died, and the fourth was sacrificed in what was obviously the terminal stage of the disease. The two pigs receiving the saline-mucin suspensions died in four days and one week, respectively. Of the two animals inoculated with the saline (no mucin) suspension, one died in 10 days, and the other was killed in extremis on the 11th day. The acid-fast fungus was recovered from the peritoneal fluid and lesions on the omentum of one of the mucin-organism injected pigs and of one of the two animals injected with the organisms alone.

Effect on the Chick Embryo: The chorioallantoic membrane of six eight-day embryos was inoculated with 0.1 ml. of a 1:100 saline suspension of the Nocardia One of the eggs was opened on the third day after inoculation, and the embryo was alive. The remaining embryos died between the fourth and the sixth day after inoculation. Plaques were observed on the membrane. Three embryos, similarly inoculated with a stock strain of N. asteroides, died on the second day after inoculation.

Sensitivity Tests.—In vitro sensitivity tests demonstrated that growth of the fungus was not inhibited by (1) 20 mg. of sulfadiazine per 100 cc. (serial dilution tube method); (2) aureomycin (Lederle 0.05 mg. tablet-agar plate method); (3) penicillin; (4) streptomycin; (5) chloramphenicol; (6) oxytetracycline ("terramycin"); (7) bacitracin (difco® disc-agar plate method). Twenty-five per cent inhibition, as compared with control plates lacking the compound, was obtained with 1% pregnenolone acetate, using a saline suspension of the Nocardia isolated and acetone dilutions of the compound mixed in Sabouraud's agar and incubated at 30 C.

Summary of Data on the Nature of the Organism.—The organism isolated from the patient conforms in general to the characteristics of the genus Nocardia. Certain properties, including its rapid growth and colony morphology, separate it from typical strains of N. asteroides, the species it most closely resembles.

COMMENT

Mycetoma of the feet and hands due to various species of fungi is known for its chronicity and resistance to all forms of therapy. Subsequent amputation of the infected part after all methods of treatment fail is the final recourse in most cases. Infections in man due to the aerobic variably acid-fast N. asteroides are regularly resistant to all forms of therapy. Tucker and Hirsch[6] collected 34 cases from the

6. Tucker, F. C., and Hirsch, E. F.: Nocardiosis, with a Report of 3 Cases of Actinomycetes Due to Nocardia Asteroides, J. Infect. Dis. **85**:72-86 (July-Aug.) 1949

literature and added 3 cases of their own. The mortality rate appeared very high; only 5 of the 37 patients could be considered as having recovered, and all 5 received sulfonamide therapy in addition to other forms of therapy. The infection was pulmonary in 33 cases; metastatic abscesses of the brain were present in at least 11, and 1 case of mycetoma of the foot, similar to that of our patient, reviewed by Henrici and Gardner [7] in the presulfonamide era, was cured by amputation after all other therapy had failed.

It is of interest that this child with mycetoma (nocardiosis) failed to respond to any form of therapy, including the sulfonamides, for nine months and then improved dramatically when pregnenolone acetate medication was started and all other forms of therapy were discontinued. The time relationship of her response to the administration of the pregnenolone acetate suggests that this agent was responsible for her recovery. The fact that her general appearance changed in two weeks after the start of steroid therapy—i. e., increased appetite, weight gain, and lack of pain in the foot—favors this view. The most important feature of the use of pregnenolone acetate in this case was the complete lack of undesirable metabolic or toxic effects. Other steroids may prove to be more potent antifungal agents, but all others thus far utilized in man have pronounced secondary sexual and metabolic actions which limit their usefulness very decidedly. This is not true for pregnenolone acetate, which can be given in a large dosage with complete impunity.[5] It can be used without hesitation in treatment of children and adults of both sexes.

SUMMARY

Pregnenolone acetate administered orally in a dosage of 200 or 300 mg. daily for eight months (a total dose of about 60 gm.) produced an apparent cure in a case of intractable mycetoma in a child 6 years of age, thus preventing eventual amputation.

The medication in this large dosage produced no systemic manifestations and no evidences of metabolic activity or toxicity.

The organism isolated from the mycetoma was identified as an atypical strain of Nocardia asteroides.

7. Henrici, A. T., and Gardner, E. L.: The Acidfast Actinomycetes, with a Report of a Case from Which a New Species Was Isolated, J. Infect. Dis. **28**:232-248 (March) 1921.

ERUPTIVE XANTHOMA AND HYPERLIPEMIA IN GLYCOGEN STORAGE DISEASE (VON GIERKE'S DISEASE)

SAMUEL J. ZAKON, M.D.
ABE OYAMADA, M.D.
AND
I. H. ROSENTHAL, M.D.
CHICAGO

SINCE von Gierke [1] reported his two cases of glycogen storage disease in 1929, fewer than 100 cases have been reported thus far in the medical literature. Because of the rarity of the condition and the fact that we could not find any case reports in the dermatologic literature, this case of eruptive xanthoma and hyperlipemia in glycogen storage disease is deemed worthy of publication.

REPORT OF A CASE

V. K., a 4-month-old white girl, was born after a full term pregnancy and a normal delivery. Her birth weight was 2,975 gm. (6 lb., 9 oz.). During her neonatal period, the infant had diarrhea and frequent vomiting until these were stopped by change of formula. The infant then appeared to thrive up to 2 months of age. It was then noticed that she had a constantly distended abdomen and frequent stools. About two weeks prior to the admission of the patient to the hospital, the mother noticed pinhead-sized yellowish spots appearing first around the elbows and gradually in a period of two weeks spreading to the entire body. The eruption did not itch. However, the child became extremely irritable, and anorexia developed. Her weight dropped from 5,530 gm. (12 lb., 3 oz.) to 5,900 gm. (11 lb., 9 oz.). She was admitted to the hospital on May 22, 1951.

Examination of the child on admission revealed that the entire cutaneous surface was studded with discrete firm yellowish papules and nodules. The lesions were not surrounded by an inflammatory zone. The lesions were most numerous on the back of the neck, scalp, and elbows, but individual lesions were also present on the knees, soles, and buttocks. The abdomen was distended, and an enlarged liver could be palpated. The liver extended to the level of the umbilicus. The spleen was not palpable. There was no adenopathy. The temperature was 98.4 F. A clinical admission diagnosis of hepatomegaly and disseminated xanthomatosis was made. When blood was drawn for chemistry studies, it was noted that the specimen was milky and orange-colored.

Blood studies on May 22 showed 3,190,000 red cells, 9.5 gm. of hemoglobin per 100 cc., and 19,850 white cells, of which 6% were stab cells, 51% segmented neutrophiles (no eosinophiles), 42% lymphocytes, and 1% monocytes. Some of the segmented neutrophiles appeared toxic. Bone marrow studies (May 24) showed large pale cells with abundant clear vacuolated cytoplasm scattered throughout the tibial marrow. On May 23 the blood sugar level (Somogyi) was

From the Departments of Dermatology, Pathology, and Pediatrics of the Mount Sinai Hospital and from the Department of Pathology of the Chicago Medical School.

1. von Gierke, E.: Hepato-Nephromegalia glykogenia (Glycogenspeicherkrankheit der Leber und der Nieren), Beitr. path. Anat. **82**:497-513, 1929.

60 mg. per 100 cc. The carbon-dioxide-combining power on May 26 was 5.8 mEq. per liter (13 vol.%); on June 6 it was 11.15 mEq. (25 vol.%). The serum pH on May 25 was 7.29; on June 9 it was 7.38. Following are the values for fats and protein:

	Lipids				Protein			
	Total, Gm./ 100 Cc.	Phospho-lipids, Mg./100 Cc.	Cholesterol, Mg./ 100 Cc.	Esters, %	Total, Gm./ 100 Cc.	Albumin, Gm./ 100 Cc.	Globulin, Gm./ 100 Cc.	A:G Ratio
5/23/51	31	....	1,176	..	13.3	3.8	9.5	0.4
5/25/51	..	....	1,410	68	....	...	...	...
5/26/51	16	65.5	.....	..	....	...	...	...
5/29/51	..	....	285	80	....	...	...	...
At this point most of the xanthomatous lesions disappeared								
5/31/51	..	....	880	58	8.1	4.0	4.1	0.97

On May 25 the cephalin flocculation and thymol turbidity reactions were negative. The thymol turbidity test on June 9 gave a value of 7 units. The results of a glucose tolerance test on May 25 (10 gm. of glucose given orally) were as follows: fasting level 70 mg. per 100 cc., at 30 minutes 40 mg., at 60 minutes 95 mg., at 120 minutes 150 mg., and at 180 minutes 192 mg. All urine specimens during the test gave negative reactions for sugar and trace positive reactions for acetone; the quantities were not sufficient for testing diacetic acid. Other results of urinalyses were as follows:

	pH	Sugar	Acetone	Albumin	White Blood Cells	Red Blood Cells	Casts
5/22/51.....	6.5	0	0	Trace	1-2	0	0-1 granular
5/28/51.....	...	0	0	Trace	2-3	0	0
6/ 7/51.....	5.0	0	Moderate	1+	3-5	0	0-1 granular

On May 24 the temperature rose to 106 F. and was associated with chills, sweating, restlessness, rapid respirations (56 per minute), and a rapid pulse (160 per minute). The ear, nose, and throat findings were negative; the chest was clear, and the sounds were resonant. Throughout the remainder of the clinical course, except for temporary short remissions, daily spiking temperature levels continued despite various forms of therapy. The picture was regarded as due to acidosis, possibly secondary to liver damage. On May 28 the temperature still remained at 102 to 103 F. Watery frequent stools were noted. At this time it was noticed that most of the xanthomatous lesions became absorbed. The glucose tolerance test showed a fasting blood sugar level of 70 mg. per 100 cc. and at one hour a level of 192 mg. per 100 cc. By June 2, the spleen became palpable. Subsequently, the child's condition deteriorated, and she died on June 10. The preterminal picture was that of severe acidosis.

The hepatomegaly since birth, the tendency toward acidosis, the fasting hypoglycemia, the lipemia, and the ketosis suggested the diagnosis of von Gierke's glycogen storage disease.

Postmortem Examination.—Owing to the restrictions of the autopsy, examination of the organs was carried out through only a 5 cm. incision made in the upper abdomen. This 4-month-old child was pale but well developed and well nourished, weighing 5,800 gm. and measuring 58.5 cm. in the crown-heel length. A few firm, small yellowish chamois-colored nodules were seen in the skin over both elbows and at the back of the neck near the hair line; but removal of skin specimens from these areas was prohibited by autopsy restrictions. No lymph nodes were palpable externally.

The abdominal wall measured 1 cm. in thickness in the midline; no subcutaneous fat was present. The peritoneal lining was smooth. A small amount of fluid was found in the peritoneal cavity.

The liver was tremendously enlarged, weighing 810 gm. (normal 160 gm.). Its lower edge was sharp and was 10 cm. below the xiphoid process and 8 cm. below the right costal border in the midclavicular line. The outer surface was smooth. The consistency was somewhat decreased. The sectioned surface was pale, with a yellowish mottling from which exuded milky, watery material. Microscopic sections revealed that the usual lobular pattern was obscured because of the great narrowing or obliteration of the sinusoidal spaces by greatly enlarged liver parenchymal cells resembling plant cells and containing abundant pink granular

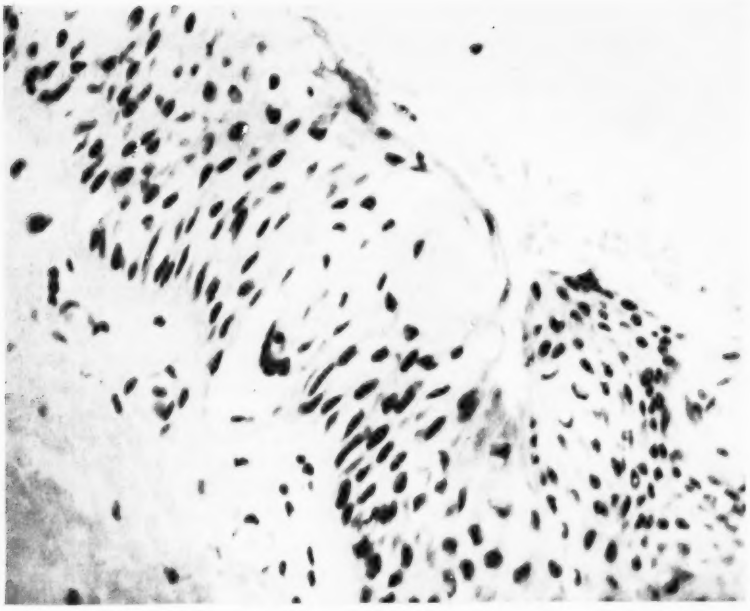


Fig. 1.—Section from a skin biopsy specimen taken on May 24. The epidermis showed diffuse, rather indefinite changes in the cells, which were enlarged, rounded, and pale, some having a signet-ring nucleus. The biopsy specimen measured only 1 by 1 mm. in its greatest dimensions, and consequently stains for fat could not be carried out. It is quite possible that the large signet-ring cells contained lipids in the presence of the tremendous hyperlipemia; hence the picture would be compatible with that of an absorption xanthoma. × 550. (Photograph supplied by the department of pathology, Mount Sinai Hospital, Chicago.)

Fig. 2.—Section from liver of patient with glycogen storage disease. The plant-like cells were loaded with glycogen; the large globoid cells were filled with fat, as shown by special stains. Hematoxylin and eosin; × 150. (Photograph supplied by the department of pathology, Mount Sinai Hospital, Chicago.)

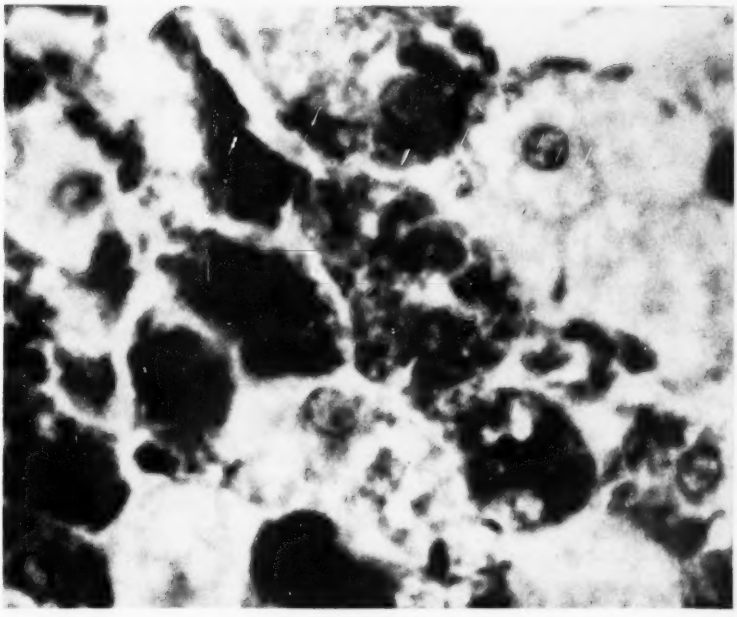


Fig. 3.—Section of liver from patient with glycogen storage disease. The plant-like cells showed numerous glycogen granules in the cytoplasm, seen as coarse dark areas in the photograph. The large globoid cells of fat exhibited a negative reaction to this stain. Best carmine stain; × 825. (Photograph supplied by the department of pathology, Mount Sinai Hospital, Chicago.)

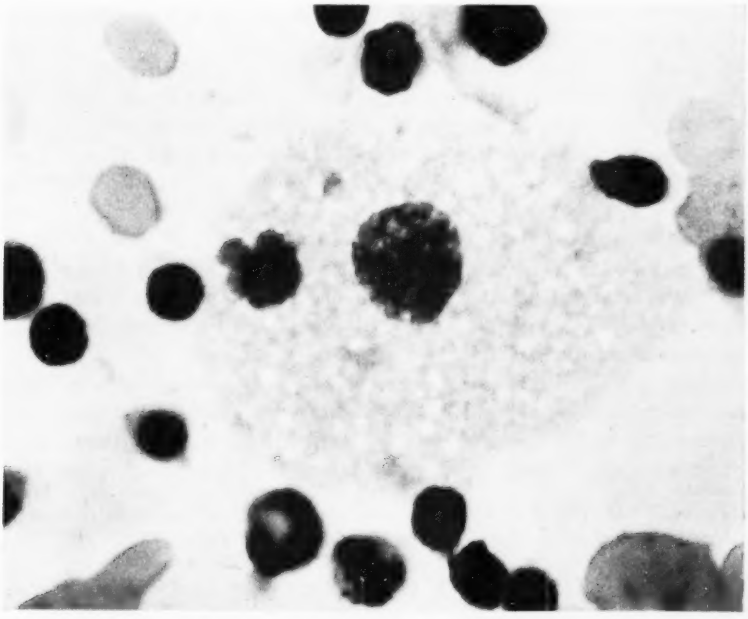


Fig. 4.—Smear of bone marrow aspirated from the left tibia during life (May 24). In the marrow were large pale cells, such as the one illustrated, in which there was abundant cytoplasm filled with clear vacuoles. At first these cells were interpreted as Niemann-Pick cells, but after the necropsy they were reinterpreted as lipid-laden reticuloendothelial cells. Similar cells in smaller numbers were found also in the lymph nodes and in the spleen in the necropsy material. × 1,250. (Photograph supplied by the department of pathology, Mount Sinai Hospital, Chicago.)

cytoplasm. With special stains for glycogen (Best's carmine) on alcohol-fixed tissue, the cytoplasm of these cells was found loaded with glycogen granules. There were also other cells in the central one-third or one-fourth of the hepatic lobules. The latter cells were globoid; their colorless or vacuolated cytoplasm took on a positive reaction with fat stains (Sudan IV) on frozen section material. There were no periportal or capsular changes of significance.

The kidneys were also increased in size; they weighed about 70 gm. (normal 43 gm.). The outer surface was smooth and pink. The consistency was moderately firm. On the cut surface the cortical and medullary structure was normal. Microscopic sections revealed the changes to be confined to the epithelial cells of the convoluted tubules. These cells were enlarged, pale, polygonal, and tall. As in the liver, they resembled cells found in plant tissue. With special stains for glycogen, numerous glycogen granules were demonstrated within the cytoplasm of these cells.

Glycogen stains were also carried out on tissues from the heart and striated muscle and showed no excessive deposits of this material in these areas.

Microscopic sections of a lymph node disclosed within the normal architecture several large phagocytic cells with a pale foamy cytoplasm lying in sinusoidal spaces. Histologic study of the spleen also showed many similar large phagocytic cells. These cells were best seen in Zenker-fixed tissues, and they resembled those seen in the smears of the tibial marrow aspirate taken during life.

Examination of the brain and thyroid was not permitted in the postmortem examination.

Anatomic Diagnoses.—The diagnoses were (1) glycogen storage disease of the liver (von Gierke) with fatty change and acute passive congestion; (2) glycogen storage disease of the kidneys (von Gierke) and acute passive congestion; (3) edema and early focal acute bronchopneumonia; (4) edema of the gall bladder and (5) acute passive congestion of a lymph node with edema.

COMMENT

Von Gierke's glycogen storage disease of the hepatonephromegalic type is an example of "scarcity in the midst of plenty." Though there is an abundant supply of carbohydrates in the form of liver glycogen, it is not broken down very easily, and the result is a hypoglycemic blood level.[2] It is believed that the patient with glycogen storage disease is lacking some of the enzyme systems necessary to break down the liver glycogen. Hence, the most characteristic feature of this disease is the extensive enlargement of the liver without enlargement of the spleen. The liver may fill two-thirds of the abdomen, causing extensive distention. The hyperlipemia and a creamy serum are observed in many cases. A low blood sugar is another cardinal feature of the serum in von Gierke's disease.

The diagnosis of von Gierke's disease is based on the following clinical features: (1) enormous enlargement of the liver without enlargement of the spleen and without signs of portal congestion; (2) hypoglycemia with hypoglycemic attacks, and (3) ketonuria and hyperlipemia.[3]

The presence of the large, lipid-laden, reticuloendothelial cells in the bone marrow, spleen, and lymph nodes would also place this case in the group of cases of secondary xanthomatosis, secondary to the hyperlipemia observed in some cases of glycogen storage disease.[4] For example, the enlargement of the liver was due

2. Bridge, E. M., and Holt, L. E., Jr.: Glycogen Storage Disease: Observations on the Physiology of 2 Cases of the Hepatic Form of the Disease, J. Pediat. **27**:299-315, 1945. Van Creveld, S.: Glycogen Storage Disease, Medicine **18**:1-128, 1939.

3. Langewisch, W. H., and Bigler, J. A.: Disorders of Glycogen Metabolism, with Special Reference to Glycogen Storage Disease and Galactosemia, Pediatrics **9**:263-279, 1952.

4. Beerman, H.: Lipid Diseases as Manifested in the Skin, M. Clin. North America **35**:433-456, 1951.

not only to excessive deposition of glycogen but also to the deposition of fat. Krakower [5] (1936) and Heller and Schwartzman [6] (1950) stressed the disturbances in fat metabolism accompanying glycogen storage disease in many cases. Thus, the presence of excessive amounts of fat in tissue does not necessarily rule out the possibility of glycogen storage disease.

SUMMARY

A case of von Gierke's glycogen storage disease is reported. Xanthomatosis and hyperlipemia were the manifestations of this rare metabolic anomaly.

5. Krakower, C.: The Lipoid Factor in Glycogen Storage Disease, J. Pediat. **9**:728-743, 1936.

6. Heller, T. M., and Schwartzman, J.: von Gierke's Disease: Report of Case with Marked Hypercholesterolemia, Arch. Pediat. **67**:197-204, 1950.

BULLOUS KERATOGENOUS AND PIGMENTARY DERMATITIS WITH BLOOD EOSINOPHILIA IN NEWBORN GIRLS

Report of Four Cases

G. ASBOE-HANSEN, M.D.
COPENHAGEN, DENMARK

THE FOUR cases reported below were so alike in appearance and course that the patients were undoubtedly suffering from the same disease, a disease which does not seem to have been described previously in dermatological or pediatric literature and which cannot be satisfactorily classified under a known diagnosis.

The first two cases have already been reported by me[1] as dermatitis herpetiformis Duhring. To these cases I can now add that of a younger sister of the patient in Case 1, who exhibited the same syndrome, though not as severely, and another case, presented before the Danish Dermatological Society on March 5, 1952.

CASE 1.—The patient was born in a municipal lying-in department in Odense at term; delivery was normal. The baby was a first-born child. The weight at birth was 3,800 gm. The parents were healthy, and there was no instance of consanguinity in the family. The pregnancy had been normal, but there was profuse bleeding after delivery. The infant was fed with a nurse's milk for a few days after birth and then was given cow's milk. Except for prophylactic instillation of silver nitrate (Credé) into the eyes at birth, no medicaments were administered, particularly not iodine.

Seven days after birth an eruption developed on the trunk and extremities, consisting in some places of papules, in others of vesicles and bullae, and in others of pustules. While in the lying-in department, the baby was treated with potassium permanganate baths and sulfathiazole, and the erosions were painted with a 2% silver nitrate solution. As the dermatitis increased in severity despite treatment, the patient was transferred to the Odense County and City Hospital (Dermatological Section) at the age of 3 weeks and remained there from Jan. 14 to March 1, 1944. On admission the clinical examination revealed no abnormality except the skin condition.

Skin.—On the scalp there was a somewhat scaly crusty patch of eczema as large as an infant's palm. On the upper and lower limbs as well as the trunk the skin was infiltrated in places and of a varying redness. There were numerous spherical papules and vesicopapules, ranging from a pinhead to a pea in size. In some places there were groups of vesicles ranging up to pea-size, and particularly on the lower limbs, there were groups of fresh and older pustules, some of which were almost dry, while others had ruptured and were covered with yellowish crusts. The eruption was most marked on the limbs, especially the legs. It was localized symmetrically, in peculiar longitudinal strands, in places quite linear.

During the first weeks the baby was always somewhat restless and crying. On the first days after admission, explosive vomiting occurred a few times; later occasional spitting occurred. The stools were completely normal all the time.

From the Rudolph Bergh Hospital (Chief: Aage Kristjansen, M.D.); the Odense County and City Hospital, Medical Department (Former chief: Knud Schroeder, M.D.), and Pediatric Department (Chief: J. Flamand Christensen, M.D.).

1. Asboe-Hansen, G.: Dermatitis herpetiformis Duhring hos børn: To tilfælde hos nyfødte, Ugesk. læger **109**:222, 1947.

Six weeks after the onset, the healing portions of the eruption were seen to be forming keratoses. Gradually stripes of ridge-shaped verrucous keratoses developed, at first on the feet and on the lateral aspect of both little fingers, later in a milder form in other affected parts. The patient was discharged with the keratoses 46 days after the onset of the disease. At that time, the skin was faintly pigmented at the former sites of the vesicles. The pigmentations were of rather regular contours and pale-brown.

The temperature remained normal throughout.

Laboratory Tests.—The Wassermann test was negative (the mother's Wassermann test was also negative). The urine contained no albumin, blood, pus, or sugar. The tuberculin test was negative. The hemoglobin content on admission was 139%; four weeks later it was 96%.

The red blood cell count was normal. White blood cell count on the 1st, 22nd, 43rd, and 63rd day showed 37.5, 26.5, 12, and 12% eosinophiles, respectively. The corresponding total leucocyte counts were 43,800, 31,040, 27,340, and 23,220. Other blood findings were normal.

Treatment.—Ointments were used, and vitamins A, D, and C were given.

Follow-Up.—The child was seen 19 months after discharge, and she had been completely normal during that time. Her skin was rather sensitive to sunlight. There were pigmentations of a grayish-brown color at the sites of the healed eruption; the skin was somewhat thickened and rough in one place on the right leg but was otherwise smooth and normal.

Eight years after discharge there remained traces of pigmentations, which, however, were visible only on close inspection.

CASE 2.—The patient was a firstborn girl, born in a private lying-in hospital at term; delivery was normal. The weight at birth was 3,350 gm. The parents were healthy and not related, and other members of the family were also healthy.

The baby was artificially fed (on cow's milk) from birth.

Two days after birth, a papular eruption developed on the trunk and, especially, on the limbs. As the disease progressed, the child was transferred, without any preceding treatment, to the Odense County and City Hospital (Dermatological Section), where she remained from April 30 to Aug. 18, 1945.

Skin.—The skin of the nape and of the abdomen was of a diffuse redness with small thin scales; there was also a diaper rash. Papules ranging from a hemp-seed to a pea in size were arranged in groups on the forearms and in stripes on the legs. In a few places groups of small vesicles and, particularly, vesicopapules were seen. Despite treatment with ointments, dressings, sulfathiazole, and a preparation of gastric mucosa, the skin condition continued to progress irregularly throughout the first months. There were papules, vesicopapules, vesicles, and pustules, as well as certain transitional varieties. The elements showed a tendency to group themselves, appearing on the abdomen in irregular groups and on the legs in longitudinal lines.

On the 26th day treatment with histaminase was instituted. The first injection was followed by an exanthema resembling measles, which, however, subsided within a few days; subsequent injections caused no reaction. The skin condition subsided slowly; no new elements appeared, but at the site of the old ones keratotic outgrowths began to form in the shape of small horny elevations, especially marked on the legs, where they were arranged in ridge-shaped lines and stripes. The keratoses slowly yielded to treatment with 5% salicylic acid in petrolatum. At the time of discharge, 115 days after the onset of the disease, the patient still had a hyperkeratotic stripe on the right foot. Otherwise, the skin was smooth, but with slight pale-brown pigmentation at the sites of the healed eruptions.

Ordinary clinical examination showed no other abnormality at any time. The baby thrived and showed no visceral symptoms.

Laboratory Tests.—The Wassermann test was negative. The red blood cell count was normal. The hemoglobin was 130 to 96%. The differential white blood cell count on the 15th, 36th, 45th, 52nd, 78th, and 98th day of the illness showed 40, 36, 19, 7, 5, and 6% eosinophiles, respectively. On the 15th and 52nd days the total leucocyte count was 21,730 and 19,120, respectively. Otherwise, the white blood cell findings were normal.

Follow-Up.—Six months after the onset of the disease a number of brownish pigmented patches and streaks were found, but otherwise the skin was normal. Seven years later the skin was still normal.

CASE 3.—The patient is a sister of the child in Case 1. She was born in a municipal lying-in department, the third child in the family (the second child, a boy, was healthy). Her birth weight was 3,375 gm., and her length was 51 cm. The pregnancy had been normal, but there was profuse bleeding after this delivery as after the first one. The baby was artificially fed from birth. Three days post partum she had an eruption on her arms and legs and was admitted to the pediatric department of the Odense County and City Hospital, where she remained from May 24 to July 17, 1948. On admission, she was slightly jaundiced. Her general condition was good.

Skin.—Scattered on the trunk, extremities, and head, particularly on the posterior and lateral aspects of the right leg, there was an eruption of firm, flat, yellowish, partly confluent vesicles and bullae, surrounded by a red zone. There were no erosions after rupture of vesicles and no exudation.

Ordinary clinical examination showed no abnormality except a small umbilical hernia and a small angioma on the left upper eyelid. The baby thrived well on buttermilk with 5%

Fig. 1 (Case 2).—Vesicular stage.

sugar; the vesicles dried, and no new elements appeared until the 16th day of the illness, when a single feeding of milk and water was followed by eruption of fresh vesicles. Buttermilk was given again, and the skin healed. On the 21st day of the illness vesicles appeared again after a feeding of milk and water. Thereupon, the skin affection slowly subsided; the baby tolerated buttermilk and thrived well. On the 34th day, diarrhea and vomiting occurred and the baby was somewhat restless, but at the end of four days digestion was normal again. There was slight conjunctivitis in the left eye, but the skin remained normal without any new eruption of vesicles.

On the 55th day firm, horny, warty patches were observed on a few fingers and toes and on the thighs and arms at the former sites of the vesicles. By this time, the baby could tolerate ordinary milk and water feedings.

Laboratory Tests.—Blood cell counts on the 21st, 25th, and 50th day showed 27, 40, and 10% eosinophiles, respectively. Otherwise nothing seemed abnormal. Microscopic examination of the urine showed no abnormality.

Intracutaneous allergy tests showed a faint + reaction to extracts of eggs and milk and no reaction to extracts of cereals, vegetables, and meat.

Follow-Up.—Four years later the patient had scattered patches with slight brownish pigmentation on the limbs. Otherwise the skin was normal and the child healthy.

CASE 4.—This child was born at term in December, 1951, in the University Hospital, Copenhagen. Delivery was normal. She was the second child in the family. Her birth weight was 3,500 gm., and her length was 55 cm. Her mother had had an abortion (in the third month) three years before. The parents were not related, and there was no instance of skin or allergic conditions in the family. During pregnancy, the mother had been treated for slight hypertension by sedatives. Delivery was without complications.

Fig. 2 (Case 3).—Keratotic stage.

On the fourth day of life, red patches of exanthema appeared on the legs and left arm, developing within a few days into vesicles and bullae. The disease was interpreted as pemphigus neonatorum and treated with penicillin.

On the 11th day of illness, the baby was admitted to the department of pediatrics of Sundby Hospital, Copenhagen. For a few days, she had had diarrhea, but it was stated that her mother had been taking laxatives. On admission she exhibited "bullous impetigo" on both lower limbs, the left upper limb, and the scalp. After a symptom-free period of 10 days, and 21 days after the first eruption, bullae with yellowish serous fluid, 1 to 2 cm. in diameter, developed on the left leg. A few days later a group of erythematous elements with tendency toward confluence appeared on the abdomen.

After another symptom-free period of eight days, bullae appeared again on the limbs, *inter alia* in the right palm. When a dermatologist suggested the diagnosis of epidermolysis bullosa hereditaria (dystrophic variety), the baby was transferred to the dermatological department of Rudolph Bergh Hospital.

As early as 13 days after the first eruption, it was noted that the skin over the ankles was of a leathery thickness. Thirty-two days later, thick verrucous keratotic outgrowths were noted at the sites of the healed vesicles, particularly on both legs, in the region of the knee, and on the feet. These outgrowths were raised from an infiltrated base and were sharply demarcated from the surrounding skin. Similar small outgrowths were observed on the left upper arm in the axilla. On the right thigh and left upper arm were seen pale scars flush with the skin but with red, hyperemic margins. There was no dystrophy of the nails, and no elements were seen on the oral mucosa. The epidermis appeared to be normal, not being injured by rubbing. Administration of potassium iodide did not cause renewed eruption.

Laboratory Tests.—A biopsy specimen of pigmented skin (Asboe-Hansen) showed the epidermis and corium without pathological changes and abundant elastic fibers in the connective tissue. The melanotic pigment was observed exclusively in the basal epidermic cells. A biopsy specimen of a keratotic area (F. Bang) showed nevus verrucosus and pronounced keratosis and parakeratosis. In the corium were found round-cell infiltration, exudation, and dilated blood capillaries but no nevus cells.

On the 64th and 73rd day, 16,160 and 8,840 leucocytes and 12 and 13% eosinophiles, respectively, were found in the blood. The red blood picture was normal, with 140 to 96% hemoglobin. The sedimentation rate was 1 to 2 mm. per hour. The tuberculin reaction (Moro) was negative.

Follow-Up.—Six months after the first eruption considerable subsidence of the keratoses was noted; the basal infiltration had disappeared completely. Brownish pigmentation of the skin was observed in places. One month later the skin was practically smooth. The keratoses had disappeared almost completely. Pigmentations were observed in patches and streaks at the former sites of the vesicles.

COMMENT

All four patients were girls. All were born in lying-in departments. Three were fed cow's milk before the eruption; the fourth, not until later. Two were sisters. All four had marked eosinophilia, which subsided at the same time as the vesicles. In all the cases the disease set in a few days after birth in the form of acute eruption of papules, vesicles, bullae, and pustules localized mainly on the limbs. In all four cases the lesions healed with formation of thick warty keratoses which slowly subsided, leaving scars and pigmentation.

The marked blood eosinophilia is suggestive of an allergic genesis. In three of the cases the cow's milk might have been to blame, but this cannot apply to the infant in Case 4, who was breast-fed.

While we were endeavoring to classify the syndrome under a known diagnosis, the following possibilities were considered.

Pemphigus neonatorum may be ruled out at once. The mode of onset, the course, and the response to treatment militate against it. There was decidedly no question of bacterial infection.

Epidermolysis bullosa hereditaria was suggested in Case 4. There was, however, no increased vulnerability of the skin, and the content of elastic tissue in the dermis was perfectly normal.

Systematized nevus was suggested in the keratotic and pigmentary stage, but it was ruled out by the history and course in each individual case.

The syndrome is closely approached, however, by two diagnoses, dermatitis herpetiformis and incontinentia pigmenti.

Dermatitis herpetiformis is called to mind by a number of previous publications.[2] In children its course may be acute, and, in a few instances verrucous excrescences have been reported at the sites of the healed vesicles. But this variety is extremely rare, and dermatitis herpetiformis is of extremely rare occurrence in newborn infants. Moreover, the course in Cases 3 and 4 scarcely seems compatible with this diagnosis.

Incontinentia pigmenti is a possibility that might be suggested by the vesicular stage, the formation of verrucous keratoses, and the pigmentation.[3] It is also supported by the onset immediately after birth, the familial occurrence, and by the fact that only girls were affected. On the other hand, the pigmentations were not of the slate-gray color or the irregular, bizarre shapes which characterize incontinentia pigmenti. They did not in any way predominate in the syndrome and exhibited the character of ordinary pigmentation of scars, healed bullae, and erosions. No other ectodermal defects had occurred in these infants or their families. A histological examination failed to show any abnormal distribution of pigment, which was found in the basal epithelial cells.

These cases may be varieties of the disease described by Wilson,[2d] Rothwell,[2b] and Willi and Burckhardt[2c] as dermatitis herpetiformis of the newborn; by Haxthausen[4] as lichenoid partly bullous skin affection of a newborn infant, and by Heilesen,[3c] Carney,[3a] and Epstein, Vedder, and Pinkus[3b] as incontinentia pigmenti (one of Heilesen's cases was identical with Haxthausen's case). But if they are, the pigmentary abnormality, particularly the "incontinence" of the pigment, must be interpreted as a sign which may be present at a certain stage without being of decisive diagnostic significance. Similarly the eruption of vesicles must be interpreted as a stage or a sign. The disease primarily should be given an adequate name, covering the entire syndrome.

According to the evidence available it does not seem possible to assign the syndrome with certainty to any known diagnosis.

SUMMARY

Four cases of dermatitis consisting of papules, vesicles, and pustules with a tendency to grouping, localized particularly to the extremities, and occurring in newborn girls, are reported. In all there was marked eosinophilia which subsided at the same time as the acute eruption of vesicles disappeared. Healing took place with formation of verrucous keratoses at the sites of the vesicles, and after the latter were shed there were brown pigmentation and atrophic skin.

The syndrome cannot be satisfactorily classified under a known disease.

Finsen Institute.

2. (*a*) Duhring, L. A.: Dermatitis Herpetiformis: Its Relation to So-Called Impetigo Herpetiformis, Am. J. M. Sc. **88**:391, 1884. (*b*) Rothwell: Dermatitis Herpetiformis? Pemphigus? Arch. Dermat. & Syph. **9**:646, 1924. (*c*) Willi, H., and Burckhardt, W.: Ein Fall von Dermatitis herpetiformis Duhring beim Neugeborenen, Kinderärztl. Praxis **12**:144, 1941. (*d*) Wilson, D.: Dermatitis Herpetiformis in an Infant: Report of a Case, Arch. Dermat. & Syph. **44**:58, 1941. (*e*) Asboe-Hansen.[1]

3. (*a*) Carney, R. G.: Incontinentia Pigmenti: A Report of 5 Cases and Review of the Literature, A. M. A. Arch. Dermat. & Syph. **64**:126, 1951. (*b*) Epstein, S.; Vedder, J. S., and Pinkus, H.: Bullous Variety of Incontinentia Pigmenti (Bloch-Sulzberger), ibid. **65**:557, 1952. (*c*) Heilesen, B.: Incontinentia Pigmenti: Two New Cases, Acta dermat.-venereol. **28**:544, 1948.

4. Haxthausen, H.: Lichenoid, delvis bulløs hudaffektion hos spædbarn, Nord. med. **21**:269, 1944.

ULTRASONIC VIBRATIONS

A Tool for Investigative Dermatology

H. J. TEMPLETON, M.D.
OAKLAND, CALIF.

THE VIBRATIONS or wave lengths beyond those audible to the human ear (which hears vibrations of 20 to 20,000 cps) are known as ultrasonic or supersonic vibrations.

These vibrations have interesting possibilities in the field of investigative dermatology. The purpose of my brief preliminary report is to call this subject to the attention of dermatologists, as there are few reports on it in our literature.

Ultrasonic vibrations can be produced by various mechanical or electrical methods. Inasmuch as the rate of vibrations is in the thousands of vibrations per second, the unit of measurement is the kilocycle; for example, 800,000 vibrations per second is spoken of as an 800 kilocycle frequency. The frequencies most commonly used in various biological, medical, commercial, and military applications have ranged from 100 to 1500 kilocycles.

Ultrasonic waves differ from electromagnetic ones in that they do not traverse a vacuum. They travel about four times as rapidly in oil as in air and about twenty times as fast in solids. They travel in a longitudinal plane rather than in a horizontal one. Because of this, they produce an alternating push-pull effect upon objects in their path. When one phase of the wave strikes a yeast cell, for example, the yeast cell is compressed, only to be expanded by the next phase of the wave. This produces changes in the interior of the cell, sometimes cavities, and the process is spoken of as cavitation. The changes in the cell vary from mere churning of the cytoplasm up to complete disintegration, depending upon the amount of energy applied.

The ultrasonic vibrations of my experiments were produced by an electrical oscillator acting upon a piezo-quartz crystal. Piezo-quartz crystals have the property of vibrating at their own inherent frequency when an alternating current in resonance with their frequency is applied to the surface of the crystal. The inherent frequency of each crystal depends upon its size, its thickness, and the angle at which it is cut and polished. As the crystal vibrates to and fro, the mechanical motion of its surface can be transmitted to an oil bath and waves generated therein. When a

---

Read at the Seventy-Second Annual Meeting of the American Dermatological Association, Colorado Springs, Colo., April 23, 1952.

William F. Gantvoort, formerly Research Associate at Stanford University, constructed the electrical piezo-quartz crystal generator used in these experiments and gave other assistance. The Department of Bacteriology and Experimental Pathology, of Stanford University, provided the facilities.

thin-walled test tube is immersed in this oil bath, the substances contained in the test tube vibrate at the same rate as the piezo-quartz crystal. The frequency used in most of my experiments was 800 kilocycles.

The generator which I used was a home-made one powered by two 500 watt gammatron tubes and brought into resonance with the piezo-quartz crystal by means of tuning helices, fixed and variable condensers. The plate voltage was 2,400 and the input to the crystal was 225 watts. The schematic diagram is shown in Figure 1.[1] Much more efficient, more powerful, and more easily varied ultrasonic generators are now available commercially, but the price of $500.00 to $3,000.00 is a deterrent to their use.

The arrangement of the piezo-quartz crystal, its oil bath, and the test tube is shown in Figure 2 and Figure 3. It is important to note that the walls of the oil bath are water cooled, since such cooling eliminates the possibility that an undesirable factor, heat, will enter into the experiment, for the generation of energy in the oil bath is accompanied by considerable heat.

When suspensions of red blood corpuscles or yeasts are subjected to ultrasonic vibrations of 800 kilocycles they can be totally disrupted. The same is true of various

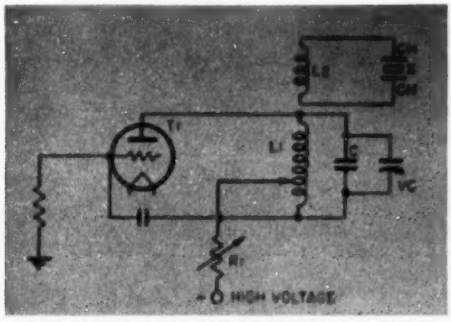


Fig. 1.—Schematic drawing of electrical hook-up of ultrasonic generator.

bacteria, such as Spirillum rubrum. Beard and Gantvoort [2] were able to partially or totally disrupt various organisms and to strip some of their capsules. Stanley [3] reports inactivation of the tobacco mosaic virus. An extensive bibliography of ultrasonics appears in the writings of Nelson, Herrick, and Krusen.[4]

EXPERIMENTAL STUDIES

EXPERIMENT 1.—Rabbits were inoculated intratesticularly with serum from human chancres. When large syphilomas had developed, the testes were removed, ground up with sterile sand and isotonic sodium chloride solution, and filtered through sterile gauze, and the resulting filtrate was used immediately for experimental purposes.

1. Figures 1 and 2 were copied from *Ultrasonics* (Bulletin No. 37, Televiso Corporation, Chicago, 1947). This bulletin gives valuable information about ultrasonic waves and has a valuable bibliography.

2. Beard, P. J., and Gantvoort, W. F.: The Biologic Effects of Supersonic Vibrations, J. Bact. **35**:5; **36**:268, 1938.

3. Stanley, W. M.: Effect of Supersonic Radiation on Tobacco Mosaic Virus, Science **80**:339, 1934.

4. Herrick, J. F.: Some Biologic Aspects of Ultrasonics, Arch. Phys. Med. **30**:145-149, 1949. Nelson, P. A.; Herrick, J. F., and Krusen, F. H.: Ultrasonics in Medicine, ibid. **31**:6-19, 1950.

When this filtrate was subjected to ultrasonic vibrations (800 kilocycles) the formerly actively motile treponemes could be broken down to intermediate lengths or completely destroyed. It was found that a 5-second exposure reduced them to about one-third of their usual length and a 10-second exposure caused them to disappear almost entirely. After 15 seconds of vibration none could be seen. This filtrate, in which no treponemes could be seen, was injected into the testicles of a rabbit. Three more rabbits each received injections of a portion of this suspension which had been vibrated further for 5, 10, and 15 minutes, respectively. In all the rabbits with

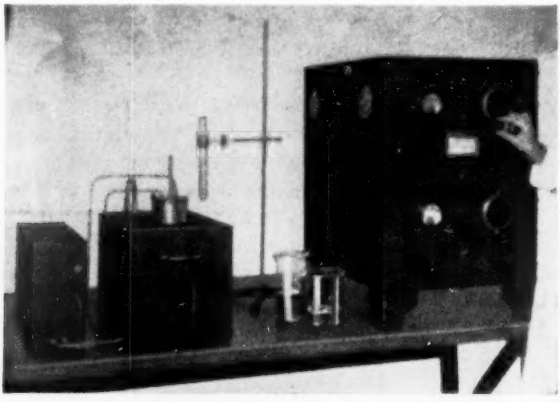


Fig. 2.—Commercial ultrasonic generator.

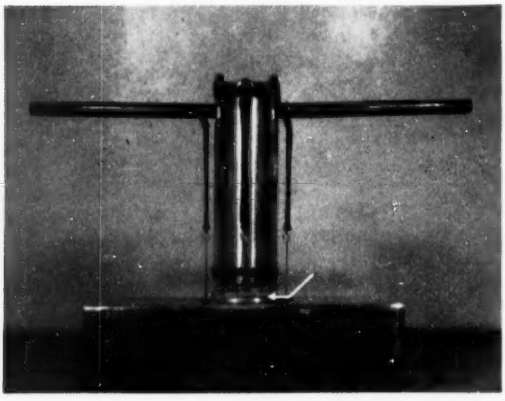


Fig. 3.—Ultrasonic transducer, water-cooled. Position of crystal indicated by light arrow.

the exception of the one injected with the five-minute-treated suspension syphilomas of the testicle developed.

EXPERIMENT 2.—It has been noted by previous workers that ultrasonic vibrations are excellent emulsifiers.[1]

A. One cubic centimeter of transformer oil and an equal quantity of distilled water was agitated by 800-kilocycle ultrasonic waves for five minutes. Emulsification occurred. The emulsion was stable for three weeks.

B. Five per cent of precipitated sulfur in distilled water was treated with 800-kilocycle ultrasonic waves for five minutes. A clear solution (colloidal ?), which remained stable, resulted.

C. Five per cent of ammoniated mercury in distilled water was treated with 800-kilocycle ultrasonic waves for five minutes. A clear solution resulted, which remained stable.

COMMENT

Beyond the certainty that Treponema pallidum can be broken down to intermediate lengths or destroyed, I am uncertain as to the significance of my first experiment. A suspension of fresh, actively motile T. pallidum which had been agitated to the point where no spirochetes could be found still produced syphilis when inoculated into rabbit testes. Does this mean that minute, ultramicroscopic, fragments of the organism can produce syphilis? Or was there in the suspension one or more whole treponemes which I could not see? We are hoping to repeat these experiments, using methods of filtration and, possibly, examination of the suspension with the electron microscope.

It has been well known to previous workers [1] that oils, water, and insoluble substances can be emulsified, dissolved, or suspended by means of ultrasonic agitation. It has also been noted by others that the factor of frequency is an important one in such experiments. This was verified by my associate, H. V. Allington, who was unable to repeat the emulsification experiment when he tried to do so with another ultrasonic generator, of 5000 kilocycles frequency.

CONCLUSIONS

Ultrasonic vibrations offer an interesting tool for investigation of certain dermatologic problems, such as the disruption of living organisms and the creation of better emulsions and suspensions.

NOTE.—Frances Keddie, M.D., Associate Professor of Dermatology of the University of California and James E. Madden, B.A., of Stanford University, are continuing with me in further experiments which are being done through the courtesy of the Department of Bacteriology and Experimental Pathology, Stanford University, and the Palo Alto Medical Research Foundation, of Palo Alto, Calif. (Director, M. A. Krupp, M.D.).

ABSTRACT OF DISCUSSION

DR. ANTHONY C. CIPOLLARO, New York: Dr. Templeton was kind enough to send me a copy of his paper. I have been immensely interested in the subject of ultrasonics for several years. In one experiment, the author showed that when a filtrate which contained visible and motile treponemes was exposed to ultrasonics, such visibility and motility disappeared; yet, this filtrate was capable of producing syphilomas. I have no explanation for this, nor does Dr. Templeton. Just think how misleading this experiment could have been if Dr. Templeton had not injected the filtrate without visible and motile treponemes into the testes of experimental animals! The inference would otherwise have been that ultrasonics destroys treponemes—which it could very well do, because it destroys many other things, as I shall point out later.

In another experiment, it was shown that suspensions of ammoniated mercury and of precipitated sulfur became clear solutions after exposure to ultrasonics. Whether these solutions would be as therapeutically effective as the suspensions was not investigated. It may be of interest to know that ultrasonics have been used in Germany in the chemical industry for making emulsions and in the alcohol industry for flavoring purposes.

My real interest in ultrasonics is this: Of what practical value are these sound waves in dermatology? I have had the good fortune of discussing this subject over the past several years with members of the Council on Physical Medicine and Rehabilitation of the American Medical Association, particularly with Dr. Frank Krusen, who is Chief of the Department of Physical Medicine and Rehabilitation of the Mayo Foundation. I believe Dr. Krusen and his co-workers have had more clinical experience and have done more research on the use of ultrasonics than

any other investigators in this country. I learned from them that ultrasonics were exploited in Germany and other European countries for the treatment of arthritis, rheumatism, lumbago, and sciatica. Now the method is in disrepute abroad for two reasons. The first is that the claims for good therapeutic results were not substantiated, and the second is that untoward reactions were quite serious in many cases. The United States is virgin territory for this treatment, and unless ultrasonics are used with great caution many patients will be hurt in an irreversible way.

The science of ultrasonics is not new. Sound engineers and biophysicists have had much experience with sound waves. Ultrasonics heat up tissues in much the same way as diathermy does except more so. The contention is that it produces its beneficial effects by increasing blood and lymph circulation. The doses that are ordinarily recommended and used are sufficient to increase the temperature of the femur of the dog as much as 20 to 50 degrees (C.), to severely damage growing bones, to damage the sciatic nerve, and to produce necrosis of the intestinal wall. Besides being an extremely dangerous device, there is no critical evidence of its value in any one disease.

Finally, Krusen and his co-workers found that ultrasonics are not effective in treatment of malignant tumors and that they have a special selectivity for hair follicles and nerve tissue. The skin exposed to ultrasonics first showed hyperemia, followed by edema, vesiculation, and necrosis extending down to muscle. I know of no skin disease that might be amenable to treatment with ultrasonics.

Ultrasonics have many fascinating possibilities as a therapeutic and as a diagnostic agent, but this is not the time for dermatologists to purchase or rent this apparatus for routine clinical use. It is capable of doing a great deal of damage to many patients who could more easily and more effectively be treated with more conventional methods.

The Council on Physical Medicine and Rehabilitation of the American Medical Association is gravely concerned about ultrasonics and fears that high-powered promotional methods may put many of these machines into the hands of medical doctors, osteopaths, trainers of athletic teams, and other practitioners of the healing arts, who might cause irreversible damage to many delicate structures to which this energy is applied.

DR. H. J. TEMPLETON: Dr. Cipollaro need not apologize in the least for throwing any wet blanket or decrying any claims for the therapeutic possibility of the agent. I have never used it for treatment. I have not advocated ultrasonics for treatment, and from all I have read of it in the foreign literature, I think it is a dangerous overrated modality. I am simply advocating it as a tool for investigative dermatology. I am very happy to give what little elementary knowledge I have in the hope that some of you may be able to go on with it in your institutions.

We are hopeful of carrying this experiment further; and when I say "we," I have recently had associated with me in this work Dr. Francis Keddie, Associate Professor of Dermatology at the University of California, and James Madden, of the Palo Alto Clinic. We are hoping to repeat these experiments, using various methods of filtration and, possibly, the electron microscope.

LOCAL TISSUE REACTIONS TO CORTISONE AND HYDROCORTISONE (COMPOUND F) IN MAN

VIII. Studies of Local Therapeutic Effect of Hydrocortisone in Diseases of Skin

LEON GOLDMAN, M.D.
AND
ROBERT H. PRESTON, M.D.
CINCINNATI

WE HAVE reported previously our investigative studies concerning the detection of compound F crystals injected into the skin; the histopathology of the reactions of normal and pathologic skin to compound F; some investigative studies on the eczematous, tuberculin, and arthropod bite reactions in the skin, and the oral use of compound F in skin diseases.[1] We should like to report in this paper the results of a study of the local therapeutic effect of compound F in 460 patients observed during the past two years.

Compound F was given by needle and syringe, by the hypospray® jet injection apparatus, in various ointment vehicles, and as a suspension in various solutions. In 160 patients, compound F acetate and the free alcohol of compound F were given orally. These patients will not be included in this report.

The results with the ointments in 135 patients given compound F acetate in concentrations from 0.1 to 5.0% were disappointing save for four patients with granuloma pyogenicum, one of whom was adult and three of whom were children. No controls were used. In two instances of granuloma pyogenicum in adults there

From the Department of Dermatology and Syphilology of the College of Medicine of the University of Cincinnati.

Cortisone acetate, free alcohol compound F, and compound F acetate were furnished by Dr. Augustus Gibson, Merck and Company.

1. (*a*) Goldman, L.; Thompson, R. G., and Trice, E. R.: Cortisone Acetate in Skin Diseases: Local Effect in the Skin from Topical Application and Local Injection, A. M. A. Arch. Dermat. & Syph. **65**:117-186 (Feb.) 1952. (*b*) Goldman, L.; Preston, R., and Rockwell, E.: The Local Effect of 17-Hydroxycorticosterone-21-Acetate (Compound F) on the Diagnostic Patch Test Reaction, J. Invest. Dermat. **18**:89-90 (Feb.) 1952. (*c*) Goldman, L.: Local Effect of Compound F on Reactions to Mosquito Bites, J. A. M. A. **149**:265 (May 17) 1952. (*d*) Goldman, L.; Preston, R.; Rockwell, E., and Baskett, J.: The Inhibition of the Tuberculin Reaction and the Tuberculin Type of Inflammatory Response in the Skin by the Local Injection of Compound F (17-Hydroxycorticosterone-21-Acetate), ibid., to be published. (*e*) Symposium on Cortisone and Compound F: Local Tissue Actions and Possible Mechanisms, Dermatological Aspects, Cincinnati, May 1, 1952. (*f*) Goldman, L.; O'Hara, E. H., and Baskett, J.: The Detection of Crystals Following Local Injection of Cortisone and Compound F into the Skin of Man, Science, to be published. (*g*) Goldman, L.; O'Hara, E. H., and Baskett, J.: Histopathological Studies of the Local Effect of Compound F in Normal and Pathologic Skin of Man, J. Invest. Dermat., to be published. (*h*) Goldman, L., and Preston, R.: Oral Use of Compound F in Dermatology, J. A. M. A., to be published.

were no changes. Two patients with discoid lupus erythematosus showed some improvement after three to eight weeks' use. In seven additional patients the results with compound F acetate in ointment form were negative. Two patients with localized scleroderma appeared to show some improvement with compound F treatment, as compared to results with prolonged massage with cortisone and the control base. In a small series there was some local effect on hypertrophic granulation tissue and in contact dermatitis of the eyelids. However, it could be stated that our present type of ointments containing compound F acetate were on the whole ineffective as topical therapy.

In 23 patients compound F acetate and in a few instances free alcohol of compound F were used as dilute wet dressings or as repeated applications. The steroids were suspended in isotonic sodium chloride solution (average 1.5 mg. per ml.) and then diluted with isotonic sodium chloride solution variously 1 : 10, 1 : 100, and 1 : 1,000. Cholesterol suspensions and cortisone acetate suspensions were used as controls. It was difficult to interpret results for in the majority of instances the solutions were used in acute self-limited conditions, and areas treated with the control suspension often improved. Except for dermatitis about the eyelids and for raw oozing vesiculobullous areas in two patients, the results in the topical solution series were likewise disappointing.

The best results were obtained with the local injection of compound F acetate directly into the skin lesion. In the majority of instances 1 to 5 mg. of compound F acetate were used. Experiments are under way to determine the minimal effective local dose, which is considerably below doses of that level. It is our impression that local injection of the free alcohol of compound F of the rod-crystal type does not produce the local inhibitory effects on inflammation that compound F acetate does. Compound F of the plate-crystal type was without any effect when injected locally. Two hundred ninety patients were used in this series of cases, and local inhibitory effects were produced in eczematous, toxic (if not too severe), psoriatic, lymphomatous, and leukemic lesions. There were local inhibitory effects also in lichen planus, xanthoma tuberosum multiplex, nevoxanthoendothelioma (two cases [three lesions], results in control lesions were negative), localized scleroderma, so-called localized neurodermatitis, atopic dermatitis, sarcoid, rheumatoid nodule, granuloma annulare (no controls), early keloidal reactions, discoid lupus erythematosus, pityriasis lichenoides chronica et varioliformis acuta, elephantiasis of penis, so-called nodular nonsuppurative panniculitis (controls), arthropod bites, superficial epitheliomatosus, nevus unius lateralis, and Darier's disease. The average time for the appearance of the inhibition was about three days. In all these instances, the zone of inhibition was limited sharply to the local area of injection and was persistent, with a central yellowish streak (deposit of insoluble crystals) and a surrounding atrophic zone which showed poikilodermatous changes in some instances. The atrophy is not permanent. In superficial epitheliomatosus the inhibition was in the inflammatory response. A weaker concentration employed in recent studies showed a lower degree of these atrophic reactions. In some instances, these reactions have persisted for at least five months, save in the scalp where these local tissue reactions are much less evident. Controls used in some cases included vehicle, cortisone acetate, and cholesterol. The results in 28 cases of urticaria, histamine wheals, and dermographism were negative. In one case of vitiligo, the

results were negative. In 15 cases of alopecia areata, no definite local effects could be observed. This series is still under observation. Investigative studies are being done on local infections, but there was no change in the healing time in a recurrent digital herpes simplex nor prevention of local recurrences by the local injection of compound F acetate. The infection group is still under study chiefly to develop a technic for the local demonstration of organisms in certain granulomas. In three patients with junctional nevi, there have been no observable effects on the development and progress of the nevus, in one instance three months after the local injection of compound F acetate.

In the entire series of over 1,000 injections there were only two secondary infections observed following the local injection of compound F. One occurred in a patient with localized neurodermatitis who scratched the area causing a mild secondary infection which spread to the local area of injection, the other in a patient having psoriasis with pyoderma. In a localized scleroderma, a central noninflammatory ulceration containing compound F acetate crystals was produced by a superficial injection of 0.3 cc. containing 7.5 mg. of compound F acetate.

The mechanisms of an apparently nonspecific inflammatory inhibitory reaction in these diverse types of dermatoses are unknown. Detailed histochemical studies of these problems and of the use of radioactive compound F are now under way [18] to attempt to develop a practical type of topical therapy for the dermatologist.

SUMMARY

From a study of the local effects of compound F in a series of 460 patients, it was found that there was a definite local inhibitory inflammatory reaction in a variety of dermatoses with the exception of the urticaria-angioedema groups and some miscellaneous dermatoses. This inhibitory reaction is produced by direct local injection and not in ointment form and as yet not with topical suspensions. The local injection of the free alcohol of compound F of the rod-crystal type does reveal some but not such extensive local inhibitory reactions. Additional studies are needed to attempt to develop a practical form of compound F therapy for local use.

CORTICOTROPIN (ACTH) AND CORTISONE IN TREATMENT OF PEMPHIGUS VULGARIS

J. T. AQUILINA, M.D.
JAMES H. TOWNSEND, M.D.
ROSS IMBURGIA, M.D.
S. A. GREENSTEIN, M.D.
AND
R. L. WUERTZ, M.D.
BUFFALO

THE PURPOSE of this paper is to emphasize the therapeutic value of corticotropin (ACTH) and cortisone in treatment of pemphigus vulgaris rather than to render a critical analysis of the study of patients with this disease, since the literature contains many excellent articles on the subject, including those by Gellis and Glass,[1] Lever and Talbott,[2] and Combes and Canizares.[3]

Treatment of pemphigus vulgaris has generally kept pace with new developments in therapeutics. Before the introduction of corticotropin and cortisone, various authors reported encouraging results with aureomycin,[4] while Magner and associates[5] reported favorable results with heparin sodium (depo-heparin®). Recent reports indicate that there may be a place for corticotropin and cortisone in the

---

Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Assistant in Medicine, University of Buffalo School of Medicine, and Assistant Chief, Medical Service, Veterans Administration Hospital (Dr. Aquilina); Chief, Medical Service, Veterans Administration Hospital, now Chief Medical Officer, Veterans Administration Center, White River Junction, Vt. (Dr. Townsend); Residents in Medicine (Drs. Imburgia, Greenstein, and Wuertz).

1. Gellis, S., and Glass, F. A.: Pemphigus: Survey of 170 Patients Admitted to Bellevue Hospital from 1911 to 1941, Arch. Dermat. & Syph. **44**:321-336 (Sept.) 1941.

2. Lever, W. F., and Talbott, J. H.: Pemphigus: Clinical Analysis and Follow-Up Study of 62 Patients, Arch. Dermat. & Syph. **46**:348-357 (Sept.) 1942.

3. Combes, F. C., and Canizares, O.: Pemphigus Vulgaris: A Clinical Pathological Study of 100 Cases, Arch. Dermat. & Syph. **62**:786-802 (Dec.) 1950.

4. Philip, A. J.: Acute Pemphigus Treated with Aureomycin, Urol. & Cutan. Rev. **53**: 417-418 (July) 1949. Bettley, R. F.: Pemphigus Vulgaris Treated with Aureomycin, Lancet **1**:66 (Jan. 14) 1950. Whittle, C. H.: Pemphigus Vulgaris Treated with Aureomycin, ibid. **1**:139 (Jan. 21) 1950. Lazar, T.: Pemphigus Acutus Treated with Antibiotics, ibid. **2**:856 (Dec. 23) 1950. Bettley, F. R., and Fairburn, E. A.: Treatment of Some Bullous Eruptions with Aureomycin and Chloramphenicol, Brit. M. J. **2**:326-329 (Aug. 11) 1951.

5. Magner, J. P.; Manson, R. C., and Pepple, A.: Successful Treatment of Pemphigus with Heparin, A. M. A. Arch. Dermat. & Syph. **64**:320-326 (Sept.) 1951.

therapeutic armamentarium for this unusual and generally fatal disease. Cannon and associates [6] reported seven patients with pemphigus treated with corticotropin and/or cortisone. Two of them died; the other five improved but required treatment to prevent relapse.

It is our intent to report our results with corticotropin and cortisone in the treatment of three patients with pemphigus vulgaris, two of whom had the acute and fulminating form of the disease and undoubtedly would have died without the use of these hormones.

Fig. 1 (Case 1).—Generalized bullous lesions of acute pemphigus vulgaris on June 4, 1951. The patient was extremely toxic.

REPORT OF CASES

CASE 1.—F. M., a 58-year-old white man, entered this hospital June 2, 1951. One month earlier small, pea-sized, blisters had developed on the soles, which rapidly spread from the lower to the upper extremities, and involved the trunk. Four days prior to hospitalization he had severe bullous formation over his entire body, with extension of the lesions to the face, scalp, and neck, associated with severe pruritus.

On admission the patient was acutely ill and toxic. He presented a generalized bullous eruption involving the entire body, including the scalp, face, neck, trunk, extremities, lower abdomen, groin, and other flexural surfaces (Fig. 1). Several bullae erupted, extruding serous fluid and leaving sharply marginated erythematous areas, many of which were crusted with blood and serum. The bullous lesions varied from 0.5 to 4 cm. in diameter. The temperature

6. Cannon, A. B.; Hopkins, J. G.; Andrews, G. C.; Colfer, H. F.; Cross, P.; Nelson, C. T.; and Howell, C. M.: Pituitary Adrenocorticotrophic Hormone (ACTH) and Cortisone in Diseases of the Skin, Pemphigus Vulgaris, and Other Bullous Dermatoses, J. A. M. A. **145**:201 (Jan. 27) 1951.

was 100.8 F. rectally, pulse rate 108, respiration rate 20, and blood pressure 116/60. There were vesicular lesions in the mucous membranes of the mouth (Fig. 2). The chest was clear. The heart revealed a rapid regular rate, with a systolic murmur at the aortic area. The abdomen was slightly protuberant. The liver was enlarged to 10 cm. below the right costal margin. There were ankle edema (1 +) and a trace of sacral edema. Findings on neurological examination were normal.

Initial laboratory findings disclosed a white blood cell count of 9,600 per cubic millimeter, with a differential count of 17% band forms, 35% segmented cells, 8% lymphocytes, and 40% eosinophiles. The red blood cell count was 3,700,000 per cubic millimeter, hemoglobin 9.4 gm. per 100 cc., hematocrit reading 34%, and sedimentation rate 47 mm. per hour. The fasting eosinophile count was 2,000 cells per cubic millimeter. Nonprotein nitrogen was 22 mg. and fasting blood sugar was 91 mg. per 100 cc. Total serum proteins were 3.5 gm. per 100 cc., consisting of albumin 1.8 gm. and globulin 1.7 gm. A direct van den Bergh test gave a negative reading; an indirect test gave a reading of 0.63 mg. of bilirubin per 100 cc. of serum. Cephalin

Fig. 2 (Case 1).—Vesicular and bullous lesions in mucous membranes of the mouth on June 24, 1951.

flocculation was negative. The reading on a thymol turbidity test was 6.4 units. A sulfobromophthalein (bromsulfalein®) sodium test revealed 20% retention of the dye at the end of 45 minutes. The Wassermann test was negative. The urine was normal except for occasional trace to 1 + reaction for albumin. Blood culture was negative. Microscopic examination of the fluid obtained from the bullae revealed rare leucocytes and rare Gram-positive cocci in pairs. A hemolytic Staphylococcus aureus (pathogenic strain) and Staphylococcus epidermidis were recovered on culture of the bullous lesions.

On June 5, corticotropin therapy by intravenous injections was started. The patient was given an initial dose of 20 mg. of corticotropin in 1,000 cc. of 5% dextrose in distilled water, administered by slow drip over a six- to eight-hour period. Wet dressings of aureomycin solution were applied, and a transfusion of whole blood was given. In view of the patient's overwhelming toxemia, low serum proteins, and loss of serum through erupted bullae, it was decided to treat him as though his were an acute burn case. Accordingly pressure dressings were applied over his entire body, in an attempt to conserve body heat and fluid. Petrolatum

gauze impregnated with bacitracin ointment was used to combat secondary infection of the skin. Plasma was administered daily, and corticotropin was increased to 30 mg. daily by continuous intravenous drip of 10 mg. every eight hours day and night. In addition he was given a high protein diet with supplementary protein feedings. Under this intensive and vigorous regimen the patient became afebrile and felt markedly improved within a few days.

On June 15, when the dressings were removed, all lesions were involuting. Fasting eosinophile counts at that time were 0 to 15 cells per cubic millimeter. The white blood cell count was 6,400, with 16% band forms, 70% segmented cells, 11% lymphocytes, and 3% monocytes. The red cell count had risen to 5,300,000, the hemoglobin to 14 gm. per 100 cc., and the hematocrit reading to 53%. Urinary 17-ketosteroid excretion was 16.3 mg. in 24 hours. Serum

Fig. 3 (Case 1).—Hyperpigmentation at sites of previous bullous lesions during ninth week of intravenous corticotropin therapy (Aug. 9, 1951).

chlorides (as sodium chloride) were 574 mg. per 100 cc. An electrocardiogram revealed prolongation of the Q-T interval. Inverted and flat T waves were consistent with hypokalemia.

On June 19, the patient went into severe congestive failure. Consequently all intravenous fluids were withheld, and corticotropin was administered by intramuscular route, 25 mg. every six hours. Intravenous injection of corticotropin was resumed June 22, at the rate of 20 mg. over a 10-hour period. Cardiac therapy was discontinued June 29, when compensation was fully restored. After July 4, the dosage of corticotropin varied between 15 to 20 mg. daily, but occasional new bullae appeared on the arms and trunk. Accordingly, the dose was increased to 25 mg. daily and subsequently increased to 30 mg. a day, which was finally determined to be the amount necessary to prevent occurrence of new lesions. By Aug. 9 all lesions had involuted, leaving only areas of hyperpigmentation at the site of the previous bullous formation (Fig. 3). However, signs and symptoms of Cushing's syndrome developed, and corticotropin was gradually reduced until the patient received only 10 mg. every other day. On Oct. 12, after four months

of uninterrupted corticotropin therapy, it was decided to change the hormone to orally administered cortisone, in preparation for the patient's discharge. At the onset he was given 100 mg. daily in divided doses. When discharged, on Nov. 24, he was receiving 90 mg. daily, which was adequate to maintain remission.

Since leaving the hospital, the patient has been followed in our clinic and maintained on cortisone, 90 mg. by mouth daily. He is gainfully employed and has no recurrence of the disease (Fig. 4).

Fig. 4 (Case 1).—Appearance of the patient on Jan. 29, 1952.

CASE 2.—R. B., a 62-year-old white man, was admitted May 22, 1951, with a pruritic rash of three weeks' duration, which began as small blisters on the dorsal surface of the hands and spread to involve the upper and lower extremities and trunk. He is an invalid as a result of paralysis agitans (Parkinson's disease).

On admission the patient was acutely ill. The temperature was 100.6 F. rectally, and the blood pressure was 134/86. He presented a generalized vesicular and bullous eruption on the trunk, arms, and legs. Several of the lesions had erupted, extruding serous fluid and leaving

marginated, erythematous, superficial erosions of the skin. There were also vesicular lesions of the mucous membranes of the mouth. Other than for generalized muscle rigidity and spasticity of paralysis agitans, the physical examination disclosed no other abnormalities.

Initial laboratory findings disclosed a white blood cell count of 6,600 cells per cubic millimeter, with 10% band forms, 51% segmented forms, 15% lymphocytes, 3% monocytes, and 21% eosinophiles. The red blood cell count was 3,900,000 cells per cubic millimeter, hemoglobin 10.2 gm. per 100 cc., and hematocrit reading 36%. The fasting eosinophile count was 1,775 per cubic millimeter. Urinalysis, serologic studies, and blood culture gave negative results. The nonprotein nitrogen was 34 mg., fasting blood sugar 112 mg., and total serum proteins 4.7 mg. (albumin 2.7 mg. and globulin 2.0 mg.) per 100 cc. Microscopic examination of fluid obtained from bullae revealed rare leucocytes and rare Gram-positive cocci. A hemolytic Staph. aureus (pathogenic strain), Aerobacter aerogenes, and enterococci were recovered on culture.

On May 25 intravenous administration of corticotropin was started, with an initial dose of 20 mg. in 1,000 cc. of 5% dextrose in distilled water. Aureomycin solution was applied topically as wet dressings, and oxytetracycline ("terramycin") was given orally to prevent secondary infection. In addition, several pints of whole blood were administered. The patient's response to corticotropin was dramatic. Within 24 hours he became afebrile and symptomatically improved, and within 10 days the lesions began to involute. Corticotropin therapy was continued with varying dosages, sufficient to prevent development of new lesions. A dose of 10 mg. every third day was finally determined to be the amount required to maintain remission.

On Oct. 2, after more than four months of intravenous corticotropin therapy, the hormone was changed to cortisone, 100 mg. daily, in divided oral doses. Subsequent attempts were made to reduce this dose, but occasional new lesions appeared, and it was necessary to resume the original dose. By the time the patient was discharged, on April 1, 1952, the anemia was corrected, the serum proteins had risen to normal levels, and the serum sodium and potassium determinations were within normal limits. As in the first case reported, only slight hyperpigmentation remained in the areas of the previous bullous lesions.

On the maintenance dose of 10 mg. of cortisone by mouth daily, the condition is still in remission and no new lesions have developed. It is interesting to note that neither corticotropin nor cortisone have had any effect on the paralysis agitans.

CASE 3.—A. B., a 39-year-old white man, was first seen at this hospital on April 5, 1951. He gave a history of chronic pemphigus vulgaris since 1943 and reported treatment at various clinics throughout the country, without any beneficial effect. On admission he presented bullous lesions of the face, neck, arms, and chest, associated with severe pruritus. The remainder of the findings on physical examination were normal. He was given a course of corticotropin intramuscularly for 10 days, with some improvement, evidenced by subsidence of the pruritus and involution of some of the lesions. However, soon after intramuscular corticotropin therapy was discontinued the lesions reappeared. He was subsequently readmitted July 8 and Nov. 15, with acute exacerbation of the disease. On each of these occasions he received corticotropin by intravenous injection for about four weeks. Each time, the pruritus disappeared and the lesions involuted, only to return a short time later.

The patient was last admitted March 17, 1952, with another acute exacerbation. The lesions were confined to the face, neck, shoulders, and chest but were of greater intensity and severity than on previous admissions. Treatment was immediately started with corticotropin injected intravenously, and the patient received 20 mg. daily for 34 days. Within a week of the start of treatment the pruritus disappeared and the lesions began to involute. The only side-effect of corticotropin was signs of hypopotassemia on the electrocardiogram, which was present even though the patient was receiving potassium chloride by mouth. On April 22, after complete involution of the lesions, cortisone by mouth, 300 mg. daily, was prescribed, and the condition continues in remission with this relatively large dose.

COMMENT

From our experience with two cases of acute fulminating pemphigus vulgaris, we have observed that 20 to 25 mg. of corticotropin injected intravenously will effect subsidence of the temperature and pulse rate and promote a feeling of well-

being within 24 hours after initiation. Continuation of this therapy will render a "toxic" patient "nontoxic" within a week to 10 days, at which time bullous lesions will show signs of involution.

The role of supportive therapy should also be stressed in the treatment of acute pemphigus vulgaris, since lost fluids, electrolytes, plasma, and plasma proteins cannot be restored by corticotropin but must be replenished directly. The liberal use of antibiotic therapy, both parenterally and topically which we feel helps control secondary infection, is discontinued promptly when the involution of the erupted bullous lesions begins.

The only serious complication we noted with the intensive use of corticotropin was development of congestive failure in Case 1 (F. M.). This, we feel, was due to overhydration by the liberal use of fluids, plasma, and blood. The antidiuretic principle of the anterior pituitary, a contaminant in corticotropin, enhanced these factors in producing circulatory failure, which fortunately responded to quinidine, digitalis, and mercurial diuretics. Despite the episode of congestive failure, administration of corticotropin was continued by the intramuscular route for three days. The intravenous method was resumed as soon as cardiac compensation was restored. Each of the two patients with acute pemphigus received corticotropin intravenously for approximately 16 to 20 weeks, by which time there was complete involution of the disease. Thereafter in both patients the condition was kept in remission by orally administered cortisone, in doses of 90 to 100 mg. daily.

In the patient with chronic pemphigus with acute exacerbations (Case 3, A. B.) intravenous corticotropin was dramatic in controlling the severe pruritus and effecting rapid involution of the lesions, within 10 days, in contrast to the poor response to corticotropin injected intramuscularly during the first admission. During this patient's last admission, intravenous injection of corticotropin was continued for 34 days, after which he was given cortisone by mouth, 300 mg. daily, which proved sufficient to keep the disease quiescent and prevented lesions from erupting.

SUMMARY

Three cases of pemphigus vulgaris are presented. In the two cases in which the disease was acute, fulminating, and toxic corticotropin was a life-saving measure in producing remission of the disease. In both cases the condition is now in complete remission in response to treatment with cortisone by mouth, in daily dosages of 90 to 100 mg. In the patient with acute exacerbations of chronic pemphigus vulgaris the disease is now maintained in complete remission with 300 mg. of orally administered cortisone daily.

THE ACNE PROBLEM

FREDERIC T. BECKER, M.D.
DULUTH, MINN.

THE ULTIMATE goal of acne therapy is to prevent permanent disfigurement and to control the altered function of the sebaceous glands. There is lack of agreement in certain phases in the treatment of this problem; therefore I should like to review my experiences in the management of 350 acne cases, especially as to the following questions: First, is there any indication of increased androgen excretion in persons with acne as compared with normal persons of a similar age? Second, what benefits can be derived from the use of estrogenic substances? Third, are oral antibiotics useful in eliminating the infectious component, and can the most beneficial medication be determined by bacterial sensitivity tests? Last, is there any favorable effect obtained by the administration of vitamin A to these patients?

The development of acne in some persons receiving injections of corticotropin has again stimulated investigations into a possible endocrine etiology. The hormonal aspects of this condition have recently been reviewed by Way and Andrews.[1] The urinary excretion of 17-ketosteroids is increased in patients receiving corticotropin, just as it is in endocrine disorders such as Cushing's disease, adrenocortical hyperplasia, and arrhenoblastoma—conditions in which acne frequently develops. In persons of prepubescent years and in eunuchs, 17-ketosteroid levels are low, and acne is not present. The excretion level rises at puberty, especially with the development of secondary sex characteristics, and it is at this time that acne initially appears.

Zarrow and others [2] found that the amount of urinary 17-ketosteroid excretion is a reliable guide to the androgen level and that this determination closely parallels the results obtained by more laborious biologic assays. Escamilla [3] and Landau [4] found the 17-ketosteroid excretion levels of value in the diagnosis of a variety of endocrine disorders. Because many workers have cited androgen as a factor in the

From The Duluth Clinic.

Read at the Seventy-Second Annual Meeting of the American Dermatological Association, Colorado Springs, Colo., April 23, 1952.

1. Way, S. C., and Andrews, G. C.: Hormones and Acne: Clinical Evaluation of Hormonal Therapy in Adolescent Girls with Acne, Arch. Dermat. & Syph. **61**:575, 1950.

2. Zarrow, M. X.; Munson, P. L., and Salter, W. T. Y.: A Comparison of Androgens Determined Biologically and 17-Ketosteroids Determined Chemically in Urine (Normal and Abnormal), J. Clin. Endocrinol. **10**:692, 1950.

3. Escamilla, R. F.: Diagnostic Significance of Urinary Hormonal Assays, Ann. Int. Med. **30**:249, 1949.

4. Landau, R. L.: Diagnostic Significance of the 17-Ketosteroids, Am. J. Clin. Path. **19**:424, 1949.

development of acne, I made a number of 17-ketosteroid determinations, according to the method of Robbie and Gibson,[5] on persons with and without acne (Fig. 1).

Ten males, from 17 to 35 years of age, afflicted with acne showed an average excretion of 19.36 mg. in 24 hours, with a variation from 15 mg. to 28.8 mg. There was no apparent correlation of the excretion level with the severity of the disease. Normal controls for this age group averaged 18.1 mg., while those from 16 to 18 years of age averaged 13.81 mg. Likewise, females with acne averaged 12.85 mg., and normal controls 11.9 mg. Kenigsberg and others [6] found 10.9 mg. to be a mean for a group of student nurses.

If androgens are a factor in the development of acne, then one must suspect a hypersusceptibility in those persons who acquire the disease, as is suggested by Sulzberger.[7] His theory is supported by the fact that among those receiving equal

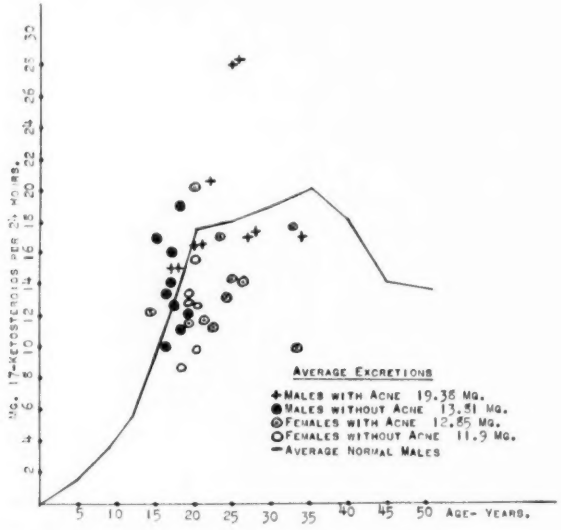

MG. 17-KETOSTEROIDS PER 24 HOURS.
2 4 6 8 10 12 14 16 18 20 22 24 26 28 30
5 10 15 20 25 30 35 40 45 50 AGE- YEARS.
AVERAGE EXCRETIONS
MALES WITH ACNE 19.36 MG.
MALES WITHOUT ACNE 13.51 MG.
FEMALES WITH ACNE 12.85 MG.
FEMALES WITHOUT ACNE 11.9 MG.
AVERAGE NORMAL MALES

Fig. 1.—Average daily urinary excretion of 17-ketosteroids by both sexes with and without acne, and normal averages for males at various ages. (Average normal values for males are from Kenigsberg, Pearson, and McGavack.[6])

amounts of corticotropin, acne develops only in certain persons, and the 17-ketosteroid excretions are similar. White, Peterson, and Neff,[8] have recently performed multiple determinations of urinary 17-ketosteroids in 26 males with various degrees of acne, and have found no appreciable variation from the normal.

5. Robbie, W. A., and Gibson, R. B.: Rapid Clinical Determination of Urinary 17-Ketosteroids, J. Clin. Endocrinol. **3**:200, 1943.

6. Kenigsberg, S.; Pearson, S., and McGavack, T. H.: Excretion of 17-Ketosteroids: Normal Values in Relation to Age and Sex, J. Clin. Endocrinol. **9**:426, 1949.

7. Sulzberger, M. B., and Witten, V. H.: Hormones and Acne Vulgaris, M. Clin. North America **35**:373, 1951.

8. White, C. B.; Peterson, A., and Neff, J. C.: Urinary 17-Ketosteroids in Young Men, U. S. Armed Forces M. J. **3**:131, 1952.

A simple classification of the types of acne is a prerequisite to an evaluation of therapeutic results. In this study patients with acne were grouped into two clinical categories. In the first type, consisting of superficial lesions (comedones and papules), scars are not produced unless marked infection develops. The second type consists of nodules and cystic lesions which are more deeply seated and are frequently pustular. Pitted and atrophic scarring is a common end-result.

Before the results of estrogenic therapy in acne patients can be evaluated, it is essential to know what action the hormone has on young adults. Estrogens inhibit the gonad-stimulating function of the anterior pituitary gland; therefore, if estrogens are given immediately after menstruation in too large doses (1.0 mg. diethylstilbestrol per day), they may inhibit ovulation. Estrogens can stimulate the formation of ovarian cysts, uterine hyperemia, and thickening of the musculature of the uterus. The mammary ductule tissue and the lobule-alveolar system may proliferate, and gynecomastia may develop in certain susceptible persons on even small doses. It has always been thought that estrogens inhibit spermatogenesis, but a recent

TABLE 1.—*Dosage of Estrogens in Relation to Therapeutic Response as Expressed in Rat Units**

	Mg.	R. U.
Natural Estrogens		
Parenteral		
Estradiol benzoate	1.0	6,000
Estrone	1.0	1,250
Oral		
Estradiol	1.0	600
Conjugated estrogenic substances (premarin®)	1.25	800
Synthetic Estrogens		
Diethylstilbestrol	1.0	1,500
Monomethylstilbestrol	1.0	500
Ethinyl estradiol	0.1	1,200
Dienestrol	0.5	1,500 (?)

* Shorr, E., and Carter, A. C.: Unpublished data.

report by Herrold [9] has shown that diethylstilbestrol in doses of 0.1 to 0.2 mg. per day for four months markedly increased the sperm count in 56% of persons who were previously infertile, decreased the count in 14%, and produced no change in 30%. There is marked variation in the effect of the different oral estrogens, so that the milligram dosage should be compared with the therapeutic response expressed in rat units (Table 1).

The role of bacteria in the development of follicular plugging and pustular lesions associated with acne has been a controversial subject. Lynch [10] found cocci in the follicles but not in the inflammatory infiltrate about the sebaceous glands. He also reported no increased sensitivity to staphylococci in acne patients as compared with normal persons. Hopkins and others [11] were able to produce acneform lesions in sensitized rabbits by the injection of staphylococci. O'Brien [12] developed

9. Herrold, R. D.: Influence of Small Doses of Stilbestrol on Oligospermia, to be published.

10. Lynch, F. W.: Acne Vulgaris, Arch. Dermat. & Syph. **42**:593, 1940.

11. Hopkins, J. G.; Weld, J. T., and Huber, W. M.: Cyst Formation, Acneform Lesions, and Hair Growth Following Intradermal Injections of Staphylococci in Sensitized Rabbits, J. Invest. Dermat. **146**:339, 1951.

12. O'Brien, J. P.: Experimental Staphylococcal Folliculitis, A. M. A. Arch. Dermat. & Syph. **65**:206, 1952.

similar alterations in human beings by placing staphylococci in nutrient salt agar on the skin of the seborrheic areas. My bacteriologic studies in the 65 cases in my report revealed that the organisms cultured from acne pustules were hemolytic Staphylococcus albus in 7, and the nonhemolytic variety in 25. Hemolytic Staphylococcus aureus was found in 3, and the nonhemolytic type in 12. No bacterial growth occurred even on repeated cultures in 10 cases with evident pustules. In eight, a mixed growth of diphtheroids, etc., was found. These did not differ greatly from the flora found in the seborrheic areas of normal human skins as reported by Evans and co-workers.[13]

Because of the variable response of cocci to antibiotics, sensitivity tests were performed on 36 preparations. A simplified and rapid technique was used.[14] The purulent secretion was smeared on a blood agar plate, then four sterile soluble

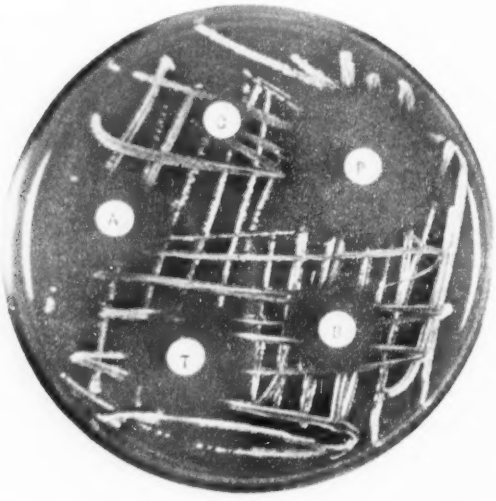


Fig. 2.—A 24-hour culture from an acne pustule (nonhemolytic Staphylococcus aureus) showing inhibitory effect of dia-discs® containing antibiotics as follows: *P*, 1 unit of penicillin G; *B*, 2 units of bacitracin; *T*, 0.01 mg. of oxytetracycline ("terramycin"); *A*, 0.002 mg. of aureomycin; *C*, 0.002 mg. of chloramphenicol.

dia-discs,® [15] each containing one antibiotic (1 unit of penicillin G, 0.002 mg. of chloramphenicol, 0.002 mg. of aureomycin, or 0.01 mg. of oxytetracycline ["terramycin"]) were placed clockwise around this plate (Fig. 2). After 24 hours of incubation the inhibitory zone around each disc was measured, and the sensitivity

13. Evans, C. A.; Smith, U. M.; Johnston, E. A., and Giblett, E. R.: Bacteria Flora of Normal Human Skins, J. Invest. Dermat. **15**:305, 1950.

14. Bondi, A., Jr.; Spaulding, E. H.; Smith, D. E., and Dietz, C. C.: A Routine Method for Rapid Determination of Susceptibility to Penicillin and Other Antibiotics, Am. J. M. Sc. **213**:221, 1947.

15. Dia-discs® are manufactured by Commercial Solvents Corporation, 260 Madison Ave., New York 16, N. Y.

TABLE 2.—*Results of Combined Therapy with Estrogens and Antibiotics in 135 Cases of Various Types of Acne**

	Cases	Age	Results: Cured	Results: Controlled	Results: No Improvement	Culture	Antibiotics	Diarrhea: +	Diarrhea: ++	Diarrhea: +++	Estrogens	Dysmenorrhea: +	Dysmenorrhea: —	Previous X-Ray Treatment
							Female							
Deep pustular.....	11	— 20	..	11	..	NSA 5	O 14	3	..	..	.....	..	..	..
						HSA ..	P 1	..	..	..	ST 23	4	3	..
	14	+ 20	1	12	1	NSAr 4	A 6	2	..	..	D 3	..	..	..
						HSAr 1	C 1	..	..	..	CE 1	..	1	15
	3	+ 30	1	2	..	Neg. 4	S ..	..	..	..	.....	..	..	..
Superficial pustular.....	14	— 20	..	12	2	NSA 8	O 12	3	1	2	ST 28	1	7	..
						HSA 2	P 1	..	..	..	.....	..	..	..
	21	+ 20	1	18	2	NSAr 3	A 7	3	1	..	.....	..	..	..
						HSAr ..	C 3	..	..	..	D 6	1	2	23
	2	+ 30	..	1	1	Neg. 1	S 1	..	..	..	CE 1	..	..	..
Deep, no pustules.....	6	— 20	..	5	1	NSA ..	O 2	1	..	..	.....	..	..	..
						HSA 1	P ..	..	..	..	ST 20	1	5	..
	9	+ 20	..	9	..	NSAr ..	A 1	..	..	..	.....	..	..	..
						HSAr ..	C ..	..	..	..	D ..	..	..	13
	8	+ 30	..	8	..	Neg. ..	S ..	..	..	..	CE 3	..	1	..
							Male							
Deep pustular.....	15	— 20	..	14	1	NSA 11	O 16	3	..	1	.....	..	..	..
						HSA 2	P 3	..	..	..	ST 29	..	..	..
	8	+ 20	..	8	..	NSAr 4	A 7	2	2	..	.....	..	..	..
						HSAr 2	C 5	..	..	..	D ..	..	..	21
	8	+ 30	1	7	..	Neg. 1	S 2	1	..	..	CE ..	..	..	..
Superficial pustular.....	8	— 20	..	7	1	NSA 1	O 5	1	..	1	.....	..	..	..
						HSA 2	P 2	..	..	..	ST 13	..	..	..
	6	+ 20	2	4	..	NSAr 1	A 2	1	..	..	.....	..	..	..
						HSAr ..	C ..	..	..	..	D ..	..	..	10
	..	+ 30	..	..	..	Neg. 2	S ..	..	..	..	CE ..	..	..	..
Deep, no pustules.....	..	— 20	..	..	..	NSA ..	O 1	..	..	..	.....	..	..	..
						HSA ..	P ..	..	..	..	ST 2	..	..	..
	1	+ 20	..	..	1	NSAr ..	A ..	..	..	..	.....	..	..	..
						HSAr ..	C ..	..	..	..	D ..	..	..	1
	1	+ 30	..	1	..	Neg. ..	S ..	..	..	..	CE ..	..	..	..

* Key to abbreviations: NSA, nonhemolytic Staphylococcus albus; HSA, hemolytic Staphylococcus albus; HSAr, hemolytic Staphylococcus aureus; O, oxytetracycline; P, penicillin; A, aureomycin; C, chloramphenicol; S, meth-dia-mer-sulfonamides; ST, diethylstilbestrol; D, dienestrol; CE, conjugated estrogenic substances.

of the organism was then determined by a table which transposed the diameter of the zone to a factor previously determined to correlate the variations in diffusibility. The organisms were scored as resistant, sensitive, or highly sensitive. In my cultures the bacteria were highly sensitive to penicillin in 11, moderate in 8, and resistant in 9; and, in like fashion, to oxytetracycline in 4, 14, and 6; aureomycin 2, 10, and 12; chloramphenicol 0, 8, and 19, respectively. This procedure, however, did not prove to be clinically helpful, as the most effective drugs were found to be aureomycin in 23 cases and oxytetracycline in 50, but gastrointestinal disturbances were so severe in 11 instances that the aureomycin and oxytetracycline medication had to be discontinued. Oral penicillin was used in eight, and chloramphenicol in nine cases; they were somewhat less effective, but no adverse reactions occurred.

The favorable effects noted in patients with indolent acne who were given oral antibiotics for some intercurrent illness and Andrews'[16] presentation prompted my investigation of the usefulness of these drugs and of estrogenic substances. During the past 18 months, 135 patients with acne have been treated with various antibiotics and estrogens; 83 of these had had relapses after maximum roentgen therapy. Crawford and his group[17] found 60 to 75% of their patients cured by adequate radiation therapy; therefore 60% of my cases were of the recalcitrant variety. In the deep nodular, cystic, and pustular types of moderate to severe degree, there were 28 females and 31 males—26 under 20 years, 22 between 20 and 30, and 11 over 30 years of age. In the females diethylstilbestrol in doses of 0.25 mg. to 0.5 mg. was given daily seven days after completion of the menses until the onset of the next period. In order not to disturb the menstrual cycle and ovulation, it is important to use this interval. In four patients nausea developed and the medication was changed either to dienestrol, 0.1 mg., or conjugated estrogenic substances (premarin®), 0.625 to 1.25 mg. The dosage was regulated by the effect on the menstrual exacerbation of the acne, and if there was no improvement, the dosage of the estrogenic substance was doubled. In four patients the dysmenorrhea became severer, in four others it was much improved, and in the rest it was unchanged.

All males tolerated 0.25 mg. to 1 mg. of stilbestrol with only an occasional case of gynecomastia developing. After a favorable response, in three to four months, the estrogen was given only three weeks per month and, if no relapse occurred, was reduced one-half and after six months discontinued, to be resumed only if sebaceous activity reappeared. Eighty per cent of the women and all the males needed the addition of an antibiotic to control the eruptions. Either aureomycin or oxytetracycline was given, 250 mg. every six hours with skimmed milk or cultured buttermilk for eight doses, then twice daily. If in one week a favorable response occurred (reduction of pustular element), then 50 mg. before meals and at night for four weeks was prescribed. If gastrointestinal symptoms developed or no response occurred, then either chloramphenicol in similar amounts or penicillin G (pentids®), 200,000 units four times a day, were used. My experience with meth-dia-mer-sulfonamides (terfonyl®) has been too limited to draw any conclusions. An effective antibiotic

16. Andrews, G. C.; Domonkos, A. M., and Post, C. F.: Treatment of Acne Vulgaris, J. A. M. A. **146**:1107, 1951.

17. Crawford, G. M.; Leukart, R. H., and Tilley, R. F.: Roentgen Therapy in Acne, New England J. Med. **245**:726, 1951.

reduced the pustular element and greatly facilitated early improvement; however, relapses were frequent after discontinuance of the antibiotic and necessitated repeated courses. Of this group, the acne was controlled in 53 patients (as shown by a marked reduction in nodules and pustules), 3 were cured, and in 2 treatment failed completely. This method appears to be satisfactory, especially in those in whom acne developed after 20. Estrogens are of value in females of this age or younger, particularly those experiencing marked exacerbations just before or during menstruation, and in those with accentuation of the lesions about the lower part of the cheeks and the chin.

The second group of patients, those having superficial lesions (comedones or papules) with pustulation, present the most difficult therapeutic problems in my experience. Improvement tends to be transitory, and small pitted scars are frequent sequelae. There were 51 patients in this category, 37 females and 14 males; nearly all were under 30. Antibiotics were the most useful treatment but had to be repeated often. Estrogens were of little value in the men, and menstrual flare-ups were the best indications for their use in women. Thirty-three, or 60%, of this group had relapsed after radiation therapy. In 75% the disease was controlled; in 15% treatment failed, and 10% were cured after three to six months' observation.

In the last category, those with deep nodular cystic lesions without infection, there were 23 females and 2 males. In these, internal therapy was practically limited to estrogens; only four received antibiotics. All but two improved; none recovered completely; 56% had previously received x-ray treatment (Table 2).

The varying reports on the benefits of vitamin A in patients with acne prompted the administration of an aqueous dispersion of synthetic vitamin A (vitamin A palmitate [Hoffman-LaRoche] containing 5 sorethytan (20) monooleate [tween 80®] as an emulsifying agent) in doses of 120,000 to 240,000 units per day. Reports[18] have shown that this preparation is more rapidly absorbed and yields higher blood levels of vitamin A than an equal dose of the natural fish oil products or other preparations contained in an oily vehicle. Patients under this treatment were advised to continue their routine local therapy and were seen at monthly intervals. One hundred and six of the 200 treated were observed for a sufficient length of time (five months to two years) to evaluate the results. Forty-one per cent improved, and all but one of these had the papular-comedone type. The vitamin did not prevent pustular exacerbations. Nine patients were entirely cured; of these five had been therapeutic problems who previously had received the maximum roentgen therapy and many local remedies without benefit.

I agree with Sulzberger[19] that vitamin A has limited usefulness in acne. It is of aid in the management only of the comedopapular type, especially if some clinical evidence of a possible vitamin A deficiency, such as follicular keratosis about the elbows and knees, coexists. A minimum daily dosage of 120,000 units must be given from three to six months in order to obtain any benefit. There were no untoward reactions, but a few patients found the preparation unpalatable.

18. Lewis, J. M.; Bodansky, O.; Birmingham, J., and Cohlan, S. Q.: Comparative Absorption, Excretion, and Storage of Oily and Aqueous Preparations of Vitamin A, J. Pediat. **31**:496, 1947.

19. Sulzberger, M. B., and Baer, R. L.: Acne Vulgaris and Its Management, 1949 Year Book of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1950, p. 9.

COMMENT

Acne remains a therapeutic problem. I believe each case must be carefully individualized after a complete history is obtained, and physical examination and indicated laboratory procedures are carried out. Each etiologic factor, as emphasized by Sulzberger,[19] and by Stokes and Sternberg,[20] must be considered, and all measures must be taken to correct any remediable defect, such as anemia, hypothyroidism, and faulty dietary and living habits. Removal of obvious focal infections has been emphasized by Andrews,[16] and the poor dentition of acne patients has been impressive to me. Evidence still points to some endocrine disturbance, but I was unable to find any marked increase in androgen excretion as indicated by the 17-ketosteroid urinary assays. Klauder, Gross, and Hanno,[21] however, found a lower 17-ketosteroid excretion and incidence of acne in a group of syphilitics with interstitial keratitis.

Rapid control of infection is desirable in order to prevent permanent scarring, and in this the newer oral antibiotics have excellent potentialities. Unfortunately the most effective, oxytetracycline and aureomycin, produce frequent gastrointestinal upsets. During the past few months I have found that using 100 mg. of oxytetracycline or aureomycin every three to four hours (five to six capsules daily for three to four days), then three times a day for several weeks, has alleviated the adverse symptoms and has been as effective in controlling the infection as were the former higher dosages. Parenteral penicillin was a disappointment to me in the therapy of "tropical acne" during 1944 and 1945; but prolonged oral treatment, 800,000 units a day over three to four weeks, has been helpful and there have been no reactions. This is also true of chloramphenicol.

Estrogens have been helpful in controlling eruptions, especially in women in whom acne develops in their late twenties and thirties and who experience premenstrual or menstrual exacerbations. Males tolerate small doses of estrogens without untoward reactions, but they should be utilized only in the severe deep-seated eruptions and not before the age of 17 unless other therapy fails and disfigurement is likely to ensue.

After intensive use of these methods of therapy during the past 18 months, I have lately been supplementing this procedure with roentgen therapy. It has been apparent that the results have been further enhanced. Chronic acne with its disfigurement is a major problem to those afflicted, and they deserve the very best of proved therapeutic methods.

SUMMARY

1. There was no significant increase in androgen excretion as measured by urinary levels of 17-ketosteroids in patients with acne.

2. Cultures of pustular lesions showed staphylococci similar to those found on skin from the seborrheic areas of normal individuals.

3. Sensitivity tests were not helpful in determining the most favorable antibiotics to use in treatment.

20. Stokes, J. H., and Sternberg, T. H.: Factor Analysis of Acne Complex with Therapeutic Comment, Arch. Dermat. & Syph. **40**:345, 1939.

21. Klauder, J. V.; Gross, B. A., and Hanno, H. A.: Endocrine Studies of Patients with Syphilitic Interstitial Keratitis, Am. J. Syph. **35**:416, 1951.

4. The oral antibiotics—oxytetracycline, aureomycin, chloramphenicol, and penicillin G—were found to be beneficial in controlling the pustular element of acne.

5. Estrogens were found to be useful adjuncts in the management of nodular cystic lesions in both sexes, but especially in women over 25 who experienced premenstrual and menstrual exacerbations.

6. Aqueous dispersions of synthetic vitamin A (palmitate) produced improvement in 46% and complete clearing in 10% of the patients with comedopapular acne.

My associate, Dr. M. G. Fredricks, supervised many of the cases and furnished helpful comments. Mr. George Smith, supervisor of the Duluth Clinic Laboratory, aided in the performance of the chemical and bacteriological studies.

Supplies of "terramycin" were furnished by Dr. Alan Wright, of Chas. Pfizer & Company, Inc., Brooklyn; aureomycin, by Dr. James D. Gallagher, of Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.; pentids® and terfonyl® by E. R. Squibb & Sons, New York; vitamin A palmitate by Hoffmann-LaRoche, Inc., Nutley, N. Y.

ABSTRACT OF DISCUSSION

DR. MARION B. SULZBERGER, New York: I should like to say at the outset that Dr. Becker's conclusions and his deliberations, his statements, coincide completely with the experience of most of us and certainly with the experience of investigators at our school. Acne is still one of the greatest problems and its management is still the major activity of most dermatologic practices. It is, I think, undeniable that our results are much better in many of these patients than they were in similar cases just a few years ago. Moreover, despite the fact that one cannot prove the role of local infections of the pilosebaceous apparatus in acne vulgaris, the administration of antibiotics has proved to be good adjuvant treatment in many cases.

The question arises, what is the mechanism of this beneficial action? Is it not possible that the antibiotics are not acting at all as local antiseptics of the skin lesions but are acting against internal foci? One point would speak in favor of this supposition, namely, that the local application of antibiotics is not nearly as effective in acne as is their systemic administration.

I think the use of estrogens in proper amounts and dosage, as Dr. Becker has outlined, is another great addition to our acne therapy. In reference to this point I should like to emphasize once again the importance of the susceptibility of the "target organ" or organ of response. This fact was very well illustrated in our observations in patients receiving cortisone or corticotropin (ACTH) in large doses. In the younger age group (let us draw an arbitrary line for "younger" at say 30 years), the patients would tend to get acne from cortisone and corticotropin, but in the older age group, for instance in the women from 40 to 60 years of age, the patients tended not to get acne but virilism of various kinds, including beards.

That I think points out very clearly the importance of the readiness or "priming" of the target organ to respond. These patients were receiving the same hormones in the same amounts, but there appears to be something intrinsic in the age process which determines the type of follicular response. Apparently, the age of the patient in some way modifies the way in which the pilosebaceous apparatus is going to respond. In other words, there is in younger persons a greater "acne readiness," and in older persons a greater readiness to produce heavy hair.

I should like to say that in giving estrogens to females we have followed a schedule a little bit different from Dr. Becker's. Independently, we came to use about the same schedule now advocated by the group at New York Hospital (Shorr, Torre, Carter, and Klumpp) and use the same preparation they used (premarin®).

DR. STUART C. WAY, San Francisco: Dr. Becker's excellent and careful survey of the acne problem does much to evaluate our present therapeutic concepts. Because of our recent and somewhat similar studies, it is a privilege for me to be able to discuss this paper.

One should first emphasize that acne vulgaris is a disease of multiple origin. Although future research may finally point to one basic cause, our present knowledge indicates that many

contributory factors or causes exist or coexist. While some of these causes have been mentioned by Dr. Becker, there are others worthy of study and consideration.

Diet in a series of several hundred cases was carefully evaluated and found causative or partly causative in 45%. Irrespective of the type of treatment used, the withholding of such foods as milk, chocolate, oranges, nuts, grapes, and their by-products is usually beneficial, and exacerbations or recurrences are less likely to occur.

Another cause frequently overlooked comes under the heading of "psychogenic," and while I am not entirely in accord with psychiatrists, there is reason to believe that emotional and sexual inhibition factors are capable of causing an endocrine imbalance, as has been brought out in a recent study by E. Wittkower, although no claim was made that acne vulgaris could be explained on psychological grounds alone.

As to the 17-ketosteroids, while a determination of the amount excreted represents an important and worth-while study, I do not believe that the findings in a large series of cases, even though normal, should devaluate the importance of the male hormone as a causative or partly causative factor in acne.

Conservatively speaking, it is my impression that an endocrine imbalance exists in 12.5% of acne patients. Such an imbalance is not necessarily due to an excessive production of any one hormone but rather to a variation in the normal production ratio of one hormone to another. This explains why in certain individuals testosterone may prove beneficial when estrogens fail, and vice versa.

It seems in order at this time to inquire whether Dr. Becker used the male hormone in his estrogen failure cases. Studies have shown that occasionally the endocrine imbalance may be in the unexpected direction. It has been my observation that nodular cystic lesions in the male are more responsive to hormone therapy than those in the female.

Vitamins deserve mention in that while vitamin A occasionally seems to help, I have seen vitamin B produce a severe acne in individuals previously immune to the disease. Before the discussion is concluded, it should be stated that hormone therapy is not a cure-all in acne and it should be used only after the more common therapeutic methods have been tried, and then in selected cases only.

Dr. C. Fred Lehmann, San Antonio, Texas: I should like to call attention to some studies made in acne cases with reference to medication with diethylstilbestrol at the Brooke Army General Hospital. The preliminary report has already been published in the January, 1952, issue of United States Armed Forces Medical Journal by Claude White, and the second report is soon to be published. I happen to be fortunate enough to have followed a considerable number of these cases. There were 96 cases of acne studied; 26 of the patients were hospitalized.

Local therapy was the same in all groups. This was naturally better controlled in those patients that were hospitalized. Most of the doctors (there were eight dermatologists observing these patients) did not know which patients were receiving diethylstilbestrol. At the end of this study it was concluded that no correlation existed between the diminished steroid output and the progress of the acne; and further, those not receiving diethylstilbestrol did as well as those receiving this medication.

Dr. George C. Andrews, New York: I was disappointed in the results Dr. Becker showed with regard to cures, and, of course, when one is interested in a subject and believes in it as I do, one probably goes after focal infections more thoroughly than one who doesn't believe in such things or does it casually.

I have been very much interested in focal infections, as you know. Just to illustrate that point, I shall mention another subject. Just about a year ago, I had a patient come to me who had been going to Dr. Stokes in Philadelphia for five years, and before that to Dr. Howard Fox in New York for three years, two of the brightest minds in dermatology, for a chronic eruption on the hands. She had had allergy tests for foods, all kinds of x-ray treatment, and various other things, but neither of them paid any attention to the numerous articles I had written about tonsils and teeth. Nobody had looked at her tonsils. Her tonsils were meeting at the midline. She was about 45 years of age. I saw her on that one visit and made an appointment for a nose and throat man to have her tonsils removed, and that is the only time that I saw her.

I have received many letters thanking me because she is cured. I think it is very important in these cases of acne, the nodular pustular form like the one shown on the boy, to have focal infections in mind.

I believe in working along with the dentist. I work with Drs. Clarence and Fred Dunn, the dental surgeons. Any impacted tooth is infected. That is the attitude we take, and a great many of these children have impacted wisdom teeth. We see a good many cures brought about by removal of those impacted wisdom teeth and of infected tonsils, together with the use of antibiotics and other therapy that has been mentioned here. I don't think that you will cure these patients by antibiotics or by hormones if they have persistent focal infection. You must get rid of the focal infections if they are present.

DR. EDWARD A. OLIVER, Chicago: I want to say that I agree absolutely with Dr. Andrews.

Several years ago, before he published his paper, my son, who was then practicing with me, insisted on having x-rays of the teeth of many of our patients with chronic acne. At first I was inclined to scoff at this, but he insisted on having a number of patients examined by a very capable young oral surgeon, who not only took x-ray pictures of the teeth, but transilluminated them as well. To my surprise, we uncovered a large number of focal infections, and when these dead, infected teeth were removed, many cases of acne cleared up nicely. I am in hearty agreement with everything that Dr. Andrews has said.

DR. STEPHEN ROTHMAN, Chicago: Dr. Becker's paper and Dr. Sulzberger's remarks made it clear that it is not necessary to assume that acne is due to endocrine disturbances. Normal girls and boys have acne if their target organs are sensitive enough to respond to the normal pubertal hormonal constellation. In our work, measuring quantitatively the volume of sebaceous glands in the rat under the influence of different hormones, we found that (1) cortisone has no effect at all; (2) testosterone exerts a powerful growth stimulus, and (3) the effect of progesterone closely approximates that of testosterone (Haskin, Lasher, and Rothman: *J. Invest. Dermat.*, to be published). It seems that in the development of acne in girls, progesterone plays a significant role. In animal experiments it also can be shown that estrogenic hormone causes a diminution in size of sebaceous glands (Ebling, F. J.: *J. Endocrinol.* **5**:297, 1948). However, huge doses must be given in order to demonstrate the antagonistic effect of estrogens, and I doubt that comparable doses can be given therapeutically without serious harmful effects.

Dr. Becker did not mention Staphylococcus vaccines in enumerating therapeutic agents in acne. Empirically, in pustular and nodular acne I found them to be a valuable support to routine local therapy.

DR. FREDERIC T. BECKER, Duluth, Minn.: In this problem I tried to evaluate only three things: estrogens, antibiotics, and vitamin A. I agree that acne is still a therapeutic problem, and there are many factors in every case. I think that Dr. Sulzberger's article discusses the etiologic agents which must be considered in each individual. Oral antibiotics have been beneficial in controlling the pustular element, although repeated courses have been necessary. Oxytetracycline ("terramycin") and aureomycin seem to be the most effective in spite of the sensitivity studies. Unfortunately, there was a high incidence of gastrointestinal reaction. During the last few months, a dosage schedule of 100 mg. every four hours, five times a day for four days, then four times a day, has been better tolerated and nearly as effective therapeutically. Every case must be selected. Diethylstilbestrol is usually well tolerated and inexpensive, and seems to be effective in nodular-cystic acne in the male and in those females experiencing menstrual aggravation and nodular chin eruptions.

I agree that focal infection is important, especially in the teeth, tonsils, and urinary tract, and I still examine every patient thoroughly. In the article that Dr. Lehmann mentioned, there was agreement in our determinations of the urinary 17-ketosteroid excretions. I have been redoing these on certain of the patients who have been taking estrogens for four to six months. I was surprised that all of them have shown higher levels, and I haven't been able to explain this fact. Dr. Lehmann found a lower level in his series. I do not think we have found the answer to acne, and acne still remains a problem.

POLYARTERITIS NODOSA AND DERMATITIS GANGRENOSA

CAPTAIN ROBERT L. GILMAN (MC), U.S.N.
AND
COMMANDER KARL V. KAESS (MC), U.S.N.
PHILADELPHIA

POLYARTERITIS nodosa may be accompanied by skin lesions more frequently than is commonly supposed. We are here reporting a case of dermatitis gangrenosa in which previously unsuspected periarteritis nodosa was found at autopsy. The possible presence of this disease should more frequently be considered in skin conditions of the sort reported here.

The patient, a blond 18-year-old service man, was admitted to the dermatology service of the United States Naval Hospital, Philadelphia, on Nov. 1, 1949, with a scaling pruritic eruption of the feet and trunk. This had developed gradually over the preceding four weeks, and he had received mild local treatment. Within the next two weeks, the eruption spread so that it involved the abdomen, back, axillae, and groin and acted like a widespread tinea corporis. The diagnosis of tinea corporis was confirmed by study of potassium hydroxide preparations of scrapings. The condition rapidly regressed under mild fungicidal applications, and after an uneventful hospital course the patient was discharged to duty on Nov. 16. During this admission, urinalysis gave negative results; the white blood cell count was elevated to 11,800, with a shift of the neutrophiles to the left; a routine chest x-ray showed no abnormalities, and one blood pressure reading was 140/82.

The patient remained well for the first week after leaving the hospital. However, on Nov. 23, he noticed a tender swelling in the left axilla followed closely by similar swellings in the inguinal region. Within the next five days new skin lesions appeared, taking the form of acute exudative patches that appeared over the right buttock, the pubic area, the left axilla, the left external auditory canal, and the right nares. He did not feel ill, nor were the lesions greatly disabling. He was given no outside treatment but was readmitted on Nov. 28.

On this second admission, the temperature was normal, the pulse rate regular and 84 beats to the minute, and the blood pressure was 130/70. He was comfortable and did not appear acutely ill. Physical examination otherwise was mainly concerned with the skin changes. The lesions were acute, oozing, and in some instances denuded patches with necrotic and indurated borders, outlining the pubic escutcheon and extending into the inguinal folds and groin and up to the lower abdomen. Similar but smaller oozing areas, purplish and with erythematous borders and induration sharply limited to the edges, were located in the left gluteal cleft and over the right buttock. Even smaller purplish crusted lesions, impetiginous in character, were located on the anterior right thigh, the left antecubital fossa, the left axilla, the left external ear, and the right nares. The ensemble of the skin lesions superficially suggested an extensive near-gangrenous herpetic eruption with marked secondary infection. A limited regional

From the Dermatology Service, U. S. Naval Hospital, Philadelphia.

Read at the Seventy-Second Annual Meeting of the American Dermatological Association, Colorado Springs, Colo., April 25, 1952.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth are those of the writers and are not to be construed as reflecting the policies of the Navy Department.

adenopathy was present. There were no mouth or mucous membrane lesions. Blood cultures taken on admission were later reported negative. Local cultures from the suprapubic area were positive for nonhemolytic Staphylococcus albus.

Fever promptly developed and the temperature rose to 101 F. daily. The white blood cell count on admission was 22,400, rising to 29,650, with a marked shift to the left. Local treatment by antiseptic applications and wet dressings was promptly started as was parenteral injection of penicillin. The patient remained febrile, became anorectic and progressively weaker. The specific gravity of the urine remained between 1.010 and 1.017 until oliguria developed. There was a persistent albuminuria from the outset, with granular casts noted on occasion. The skin lesions remained fairly static although they showed no tendency to heal. The patient's downhill progression took place very quickly on his fourth hospital day. At this time pallor was characteristic and some generalized edema appeared. The liver was palpable 2.5 cm. below the costal margin, fine râles appeared over the left chest, and the heart was found to be enlarged 9 cm. from the midsternal line. Gallop rhythm developed. Funduscopic examination was negative. His major complaints continued to be weakness, but he had no abdominal pain. The blood pressure dropped to an average of 100/70. The smaller skin lesions had regressed; the larger pubic patch had developed a black eschar typical of gangrene. Small, frequent transfusions were being given, and aureomycin by mouth had been added to the penicillin therapy. On the eighth day of this second admission, two weeks following the onset of his second illness, upon attempting to leave his bed the patient collapsed suddenly and died in apparent cardiac failure.

At autopsy the lungs showed marked congestion and edema. Microscopically the heart showed severe myocarditis with increase in fibrous tissue and marked inflammatory cell invasion. The increase in fibrous tissue was noted especially around the blood vessels. There was slight increase in perivascular fibrosis around the coronary arteries. The brain appeared normal. There was moderate edema of the periadrenal tissue. There was severe arteritis of the smaller arteries in the periadrenal tissue with proliferation of the endothelium, adjacent inflammatory cell invasion, and increased perivascular fibrosis. The kidneys showed congestion throughout and cloudy swelling of the proximal tubules. There was thickening of the cells lining Bowman's capsules and occasional fibrosis of the glomeruli. The collecting tubules contained casts. The ensemble was that of early glomerulonephritis. The liver showed extreme acute congestion with slight fatty infiltration. There was marked congestion of the spleen with occasional small arteries showing marked fibrosis and thickened walls. In the skin the arteries showed marked arteritis. The pathologic diagnoses were polyarteritis nodosa; chronic dermatitis (early gangrene); early nephritis (acute); myocarditis; pulmonary edema; marked congestion of the liver, spleen, and lungs, and bilateral hydrothorax.

COMMENT

Soon after the patient's second admission the condition was thought to be dermatitis gangrenosa, on morphologic grounds. Polyarteritis was not suspected by us or by the medical consultants. There appeared to be no relationship between this admission and the previous one, in which the case appeared to be a well-delineated instance of widespread tinea corporis. At least local causation of tinea corporis was confirmed by the potassium hydroxide examinations. During the first admission, as well as previously and in between admissions, no drugs were given, no measures taken that might have contributed to a state of sensitization or allergy. However, one disquieting observation made by us on the second admission was the marked similarity of the extensive necrotic pubic ulcerative lesion to an example of a local Arthur phenomenon. This observation was not pursued—possibly because of the absence of any history of anaphylactoid background and the presence of associated polymorphic lesions elsewhere in what appeared to be a nonsignificant distribution.

Needless to say, subsequent to this case, polyarteritis was offered as a diagnosis for a widening range of unexplainable febrile conditions, and this is as it should be.

In fact, there is ample evidence of its increasing incidence, and it is most often recognized after death.

The part played by the skin condition, which we still choose to term "dermatitis gangrenosa," is problematical. This condition by itself is sufficiently rare and far from completely understood in etiology and significance. However, in view of the knowledge too often gained in retrospect, it may be recalled that purpura, petechia, hemorrhage, and gangrenous ulcers occurring together are the second commonest skin accompaniment of polyarteritis—second only to the classically conceived periarteritic nodule. It is to be said in passing that this latter type of lesion was not observed in the case just described.

Recapitulations of the signs and symptoms of clinical polyarteritis by several authors have stressed the predominant signs as fever, leucocytosis, renal manifestations, hypertension, edema, and abdominal pain. Skin lesions have been said to occur in about 25% of the cases, and the liver is less commonly involved. We believe that skin lesions, on more searching analysis, will prove to appear in a much greater frequency.

Despite the absence of any clear-cut previous evidence of treatment or other sensitization mechanisms, the occurrence of widely distributed, necrotic and gangrenous lesions, not otherwise easily explained, should draw prompt attention to a consideration of polyarteritis nodosa.

SUMMARY

An 18-year-old service man was admitted to the hospital with an acute pyogenic dermatitis of the buttock, pubis, axilla, ear, and nares. A limited adenopathy was present, but the patient did not appear acutely ill. The lesions progressed rapidly despite treatment to necrotizing areas, and fever developed. Blood culture was negative. Generalized weakness developed; the heart and liver became enlarged, and gallop rhythm ensued. Albuminuria appeared, and the blood pressure readings fell. Antibiotics, blood transfusions, and other therapy failed, and the patient died suddenly on the eighth hospital day. Autopsy findings were typical of a fulminating polyarteritis nodosa not previously suspected. Gangrenous dermatitis and polyarteritis nodosa should not be considered entirely disparate, but, on the contrary, their possible association should be borne in mind.

AMYLOID "TUMOR FORMATION" OF SKIN

IRVING N. HOLTZMAN, M.D.
AND
JACOB SKEER, M.D.
BROOKLYN

LOCALIZED amyloidosis is not an uncommon syndrome in medical literature. However, its appearance simulating tumor formation, particularly in the skin, is a most unusual finding. The case here presented is reported primarily for its rarity.

REPORT OF A CASE

The patient, a married woman, aged 56, a housekeeper, was first referred to the outpatient department of the Jewish Hospital of Brooklyn, by Dr. M. G. Wasch on May 14, 1951. At that time she presented a "growth" on her nose, which she claimed had been present for approximately one year. The growth, following its first appearance, had increased in size rather rapidly for about six months and then had remained stationary up to the time of examination. There were no symptoms aside from the cosmetic problem presented by its appearance.

Examination on admission disclosed a well-nourished middle-aged woman whose general physical examination presented no important abnormalities aside from the skin lesions. There was a nodular swelling on the right ala nasi, lobulated in appearance, skin-colored, about 2 cm. in diameter. A similar smaller nodule, about 5 mm. in diameter, was noted on the tip of the nose, and one of equal size on the left lower eyelid. All the lesions were rubbery in consistency to palpation.

A biopsy specimen was taken immediately, and because of the unusual findings another specimen was removed a week later. Both sections showed identical histological pictures. Microscopic examination disclosed the following findings:

The epidermis appears undisturbed except for some thinning out by pressure from an underlying process. The corium and cutis are completely displaced by a homogenous, faintly eosinophilic substance (hematoxylin and eosin stain) arranged in broad bundles, which in turn appear concentrated in lobules.

When the specimen was stained with Congo red, the specific chemical was absorbed by the homogenous substance, although not as intense as is usually seen in amyloidosis. When methyl violet stain was used, metachromatic staining of the substance was noted. Preparation with Van Gieson stain showed a yellow tinting of this deposit standing out in sharp contrast to the bright red stain of the few remaining fibrils of collagen in the surrounding corium.

The histologic diagnosis was amyloidosis of the skin. The bundle-like arrangement suggested a biochemical change in a possibly structural type of preexisting neoplasm.

From the Departments of Pathology and Dermatology, Jewish Hospital of Brooklyn.

Associate Attending Dermatologist and Dermatopathologist (Dr. Holtzman) and Attending Dermatologist (Dr. Skeer).

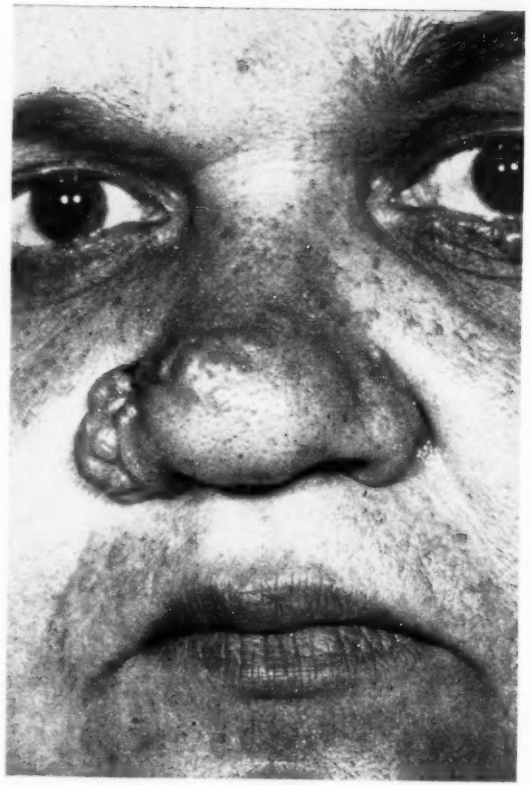


Fig. 1.—Clinical appearance of patient.

Fig. 2.—Low-power hematoxylin and eosin preparation.

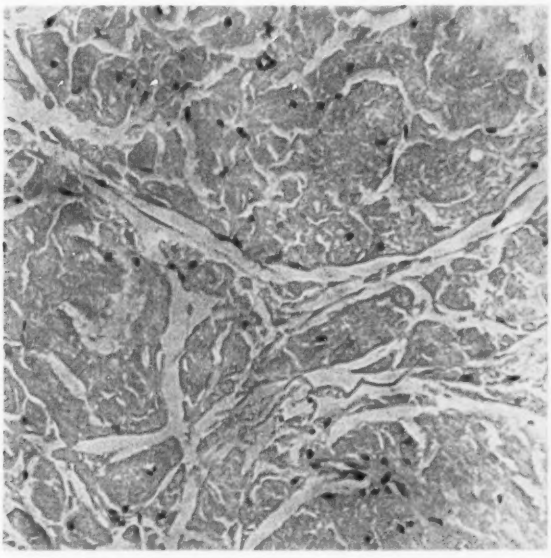


Fig. 3.—High-power hematoxylin and eosin preparation.

A specimen was removed and submitted to the department of biochemistry for chemical partition. The findings are shown in the tabulation.

	Mg	
Total weight		30.8
Total lipids		6.6
Cholesterol esters	0.0278	
Free cholesterol	0.0276	
Lipid phosphate	0.0056	
Residual fat	5.5422	
Total protein		12.60
Saline-soluble	4.92	
Albumin	3.75	
Globulin	1.17	
Saline-insoluble *	7.68	

* In the test tube this fraction of saline-insoluble protein strongly absorbed Congo red.

Careful examination by the department of medicine failed to disclose any evidence of amyloid disease in any other system.

COMMENT

It is fruitless to speculate as to the cause of this particular lesion. Aside from the possibility of the amyloid change being a degenerative one in a preexisting lesion, no other source could be disclosed. Thorough examination of all the sections taken failed to disclose any evidence of a different type of tumor such as one of the epithelial or muscle varieties seen in the skin. For this reason it is felt that we are dealing here with a primary type of localized amyloidosis of the skin itself. Whether this is purely a degenerative change with physical swelling because of the physical structure of amyloid or whether this a true amyloid-forming tumor cannot be determined from the evidence available. Again, whether this is amyloid or paraamyloid is only of academic interest.

A search of the literature has disclosed one report of a case similar to the one herein described, with a review which included three other cases, none of which involved the face. The origin of amyloid is also discussed with reference to possible derivation from elastic tissue as a degenerative phenomenon.[1]

There is also a resemblance of the picture here to the findings described under the term "colloid milium." However, there are two significant points of difference:

1. The lesion here is much larger.
2. The positive stain for amyloid is not obtained in colloid milium.

SUMMARY

A case is presented of tumor formation of the face with histologic findings of amyloidosis.

135 Eastern Parkway (17).

1. Bizzozero, E., and Midana, A.: Ann. dermat. et syph. **10**:18-24 (Jan.-Feb.) 1950.

EFFECT OF ROENTGEN RAYS ON MICROSPORUM AUDOUINI

An in Vitro Study

KURT LOEWENTHAL, M.D.
FREEPORT, N. Y.

THIS PAPER reports the effect of roentgen rays on Microsporum audouini, under experimental conditions approximating those presented in a previous study on Microsporum canis.[1] The pertinent literature was cited in the latter publication.

MATERIALS AND METHODS

Two freshly isolated strains (JC and HM) were used. Six subcultures were prepared of each strain, two of which were irradiated on the day of inoculation; two seven days after inoculation, and two remained untreated to serve as controls. The irradiation was given through the glass wall of the medium container (½ oz. [15 cc.] perfume bottles), the filtration value of which was not known. Following are the technical data: Bracke-Seib Dermatron; two-valve tube rectification; Eureka tube type 13-; 85 kv.; 5 ma.; 25 cm. distance; 3 minutes 25 seconds; 340 r unfiltered. Three successive transplants from the irradiated colonies and their controls were prepared at intervals of three weeks. The transplants were retransplanted on three occasions at intervals of three weeks.[2] The medium used was dextrose-peptone agar (difco®), slanted in test tubes for the transplants and retransplants. The individual colonies were kept under observation at room temperature for four months. At intervals of three weeks the colonies were inspected and microscopic examinations were made of particles from their centers.

RESULTS AND COMMENT

For the purpose of evaluating the results the component features of the colonies are separately discussed in terms of differences between the irradiated and control series.

1. *Rate of Growth.*—No difference was noted.

2. *Gross Structure.*—There was no difference, with the following exceptions: Once a more luxuriant surface growth in a control colony was observed (strain JC, first generation); twice a more fluffy mycelium in the irradiated series (strain JC, third and fourth generations, second transplant). These deviations were not

From the Division of Dermatology and Syphilology, State University of New York, College of Medicine, at New York City, Brooklyn.

1. Loewenthal, K.: Effect of Roentgen Rays on Microsporum Canis: An in Vitro Study, A. M. A. Arch. Dermat. & Syph. **63**:750 (June) 1951.

2. For the purpose of identification, the irradiated colonies and their respective controls were referred to as mother colonies or as colonies of the first generation, their immediate descendants as colonies of the second generation, and so forth in proper chronologic sequence. The colonies irradiated immediately following inoculation (including their descendants) were called A, the colonies irradiated seven days after inoculation (including their descendants) were called B, and the control colonies and their descendants were called C colonies.

constant and transmissible; they were present at the initial stage of the colony and/or disappeared in the subsequent generation. Once a more compact mycelial mat was recorded in the control colony (strain HM, fifth generation, third transplant). It must be noted that the variations occurred at irregular and infrequent intervals in the irradiated as well as the control series and that no hereditary trend existed.

3. *Pigmentation.*—In strain JC, the third transplant of the control from the third through the fifth generation was more pigmented than the corresponding descendants of the irradiated colony. In strain HM, however, although the control mother colony showed a slightly darker pigment than the irradiated mother colony, once (second generation, first transplant) its pigment was lighter than in both of the irradiated series and twice (second generation, third transplant, and fifth generation, second transplant) it was lighter than the corresponding A but darker than B. It must be noted that the deviations were neither hereditary nor restricted to the irradiated or the control series.

4. *Microscopic Structures, Excluding Macroconidia.*—In strain HM (fifth generation, third transplant), hyphae were more delicate and a tendency to form chains of arthrospores was less pronounced in the control than in the irradiated series. These differences tended to become indistinct at the end of the observation period. In strain JC a more delicate mycelium as well as diminished inclination to form arthrospores and chlamydospores was prevalent among the descendants of the irradiated colonies. Only once (A, fifth generation, second transplant) there seemed to be a slight preponderance of chlamydospores in the irradiated series. It should be noted that the differences were minor, not hereditary, and occurred in descendants of control or irradiated colonies.

5. *Fuseaux.*—No fuseaux were discovered in either the irradiated or the control series of strain JC. In strain HM, once a few fuseaux (second generation, second transplant) and once a moderate number (third generation, second transplant) were seen in the irradiated series, and once a few fuseaux occurred in the control series (second generation, third transplant). In these instances the medium was contaminated with a rust-colored fungus. It must be noted that fuseaux formation was erratic and not hereditary. Small numbers occurred only in one strain, at irregular and infrequent intervals, and in descendants of an irradiated as well as the untreated colony. Moreover, their occurrences coincided with the presence of a contaminating fungus. It is conceivable that there was a causal relation between this accidental contaminant and the presence of fuseaux. For instance, a unilateral stimulation of M. audouini with production of macroconidia through a bacterium was reported by Benedek.[3] However, a further discussion of this phenomenon is omitted as not relevant to this paper.

COMMENT

These observations suggest that none of the deviations noted can be interpreted as irradiation effect. A dose of 340 r of unfiltered roentgen rays apparently did not produce changes in the irradiated colonies, as well as descendant colonies, detectable by means of the methods used. A comparison with the results of the

3. Benedek, T.: Unilateral Stimulation of Microsporum Audouini by a New Species of Bacillus, Mycologia **35**:222, 1943.

previous study reveals that M. canis, treated and observed under similar controlled conditions, reacted differently.[1] Briefly, the irradiated colonies remained free from gross and microscopic changes, but some of their descendants showed accelerated pleomorphism and massive deterioration of the fuseaux formation. This difference in sensitivity to a given dose of roentgen rays would fit into the pattern of the known biologic differences of the two genera and could conceivably be correlated with fundamental facts regarding the action of roentgen rays on living cells in general. However, a conclusion and an attempt at explanation must be deferred until further, more extensive, investigations have been accomplished.

SUMMARY

Two freshly isolated strains of Microsporum audouini, growing on dextrose-peptone agar, received one exposure each of 340 r of unfiltered roentgen rays. Neither the irradiated colonies nor their descendants showed gross and microscopic changes attributable to the irradiation. In experiments previously published, Microsporum canis under similar controlled conditions revealed acceleration and intensification of pleomorphism and degradation of the fuseaux formation. Further studies are required to investigate this apparent difference in sensitivity to a given dose of roentgen rays.

STUDIES ON LICHEN MYXEDEMATOSUS (PAPULAR MUCINOSIS)

JOHN ERIC DALTON, M.D.
AND
MARTIN A. SEIDELL, M.D.
INDIANAPOLIS

LICHEN myxedematosus is now an accepted entity classified under the mucin-exhibiting diseases of the skin. It was once regarded as rare, but a number of cases are now being recorded. Refined diagnostic procedures, a sharper clinical focus, and a reevaluation of similar previously reported cases have contributed to this increase. Furthermore, variations of this picture are now recognized, and some of these will be reported by Montgomery and Underwood [1] at the next meeting of the Society for Investigative Dermatology. This report concerns two personally observed cases of the papular form of this disease.

CLASSIFICATION AND TERMINOLOGY OF CUTANEOUS MYXEDEMATOUS STATES

The diseases in which mucin is deposited in the skin may be divided into four groups.

The first group shows skin changes associated with hypothyroidism. Ord [2] (1878) coined the word "myxoedema" to describe a diffuse, nonpitting, swelling of the skin associated with thyroid deficiency. Later, variants were recognized. For example, Dössekker [3] (1916) reported the case of a man with scattered nodular-tuberose lesions which responded to thyroid implantation. Reuter [4] (1931) demonstrated an excess of mucin in the skin of persons who showed a lowered basal metabolic rate without any clinical evidence of thyroid disease. Green and Freudenthal [5] (1948) recorded a case of hypothyroidism associated with papular cutaneous lesions.

Read at the Seventy-Second Annual Meeting of The American Dermatological Association, Colorado Springs, Colo., April 23, 1952.

From the Department of Dermato-Syphilology of Indianapolis General Hospital and The Alembert Winthrop Brayton Skin and Cancer Foundation.

1. Montgomery, H., and Underwood, L.: Personal communication to the authors.

2. Ord, W. M.: On Myxoedema, a Term Proposed to be Applied to an Essential Condition in the "Cretinoid" Affection Occasionally Observed in Middle Aged Women, Med.-Chir. Tr. **61**:57-78, 1878.

3. Dössekker, W.: Über einen Fall von atypischen tuberösem Myxödem, Arch. Dermat. u. Syph. **123**:76-129, 1916.

4. Reuter, M. J.: Histopathology of the Skin in Myxedema, Arch. Dermat. & Syph. **24**:55-71, 1931.

5. Green, B., and Freudenthal, W.: Myxoedema Papulosum, Brit. J. Dermat. **60**:22-24, 1948.

The second group includes localized eruptions which are usually pretibial and symmetrical in location and which are usually associated with a hyperthyroidism of the toxic goiter type. These lesions have been termed symmetrical areas of solid edema,[6] localized solid edema,[7] circumscribed myxedema,[8] circumscribed pretibial myxedema[9] and myxoedema circumscriptum thyrotoxicum.[10]

In the third group, several types of skin lesions may occur without any demonstrable thyroid disease. Such eruptions have been designated as lichen myxedematosus,[11] mucoid papular disease,[11] generalized localized myxedema,[12] and lichen fibromucinoidosis.[13] Probably the first recorded cases in this group are those of Dubreuilh[14] (1906) and Reitmann[15] (1908). Moreover, the two cases which we report here belong in this division.

A fourth group is mentioned merely for completeness. Various neoplasms (sarcomata, fibromata, lipomata, etc.) may show excessive mucin deposition. However, such lesions are not pertinent to the subject under consideration and will not be discussed further.

Thus, universal, diffuse, generalized, or localized mucin-containing eruptions occur which are associated with either hypothyroidal or hyperthyroidal states, or which bear no demonstrable relationship to thyroid disease. The single finding common to all is the presence of mucin in the cutis. Therefore, it seems more logical to accept the idea of Palitz and Brunner[16] that these disorders are mucinoses, and to discontinue classifications based on other concepts.[17] Such a nomenclature avoids the use of the word myxedema and the other terms stemming from it, which medical usage has associated with hypothyroidism.

A classification is submitted which groups all these varied pictures under the general heading of "the mucinoses" (Table 1). For cases like those reported here, we propose the name papular mucinosis, and list them in a subgroup in which no

6. Morrow, H.: Symmetrical Areas of Solid Oedema Occurring in Graves's Disease, Brit. J. Dermat. **11**:286-288, 1899.

7. O'Leary, P.: Localized Solid Edema of the Extremities in Association with Exophthalmic Goiter, Arch. Dermat. & Syph. **21**:57-76, 1930.

8. Pillsbury, D. M., and Stokes, J. H.: Circumscribed Myxedema of the Skin, Arch. Dermat. & Syph. **24**:255-270, 1931.

9. Trotter, W. R., and Eden, K. C.: Localized Pretibial Myxedema in Association with Toxic Goiter, Quart. J. Med. **11**:229-240, 1942.

10. Cohen, E. L.: Myxoedema Circumscriptum Thyrotoxicum, Brit. J. Dermat. **58**:173-182, 1946.

11. Neumann, H.: Die Schleimpapel Krankheit (Lichen myxoedematosus), Dermat. Wchnschr. **101**:1263-1268; 1294-1299, 1935.

12. Dalton, J. E.: Generalized Localized Myxedema, Arch. Dermat. & Syph. **44**:689-691, 1941.

13. Lorincz, A.: Personal communication to the authors.

14. Dubreuilh, W.: Fibromes miliaires folliculaires: sclérodermie consécutive, Ann. dermat. et syph. **7**:569-572, 1906.

15. Reitmann, K.: Über eine eigenartige der Sklerodermie nahestehende Affektion, Arch. Dermat. u. Syph. **92**:417-424, 1908.

16. Palitz, L. L., and Brunner, M. J.: The Mucinoses: A Classification with Histochemical Studies on the Nature of Mucin, J. Invest. Dermat. **14**:150-168, 1950.

17. *(a)* Pillsbury, and Stokes.[8] *(b)* Carol, W. L.: Über atypisches Myxödem, Acta dermat.-venereol. **13**:127-149, 1932. *(c)* Scheuermann, H.: Über Hauterscheinungen mit Beziehung zu Myxödem und Basedowscher Krankheit, Arch. Dermat. u. Syph. **176**:544, 1938.

demonstrable thyroid disease or other specific endocrinopathy can be shown (Table 2). However, the term papular mucinosis cannot be applied to all cases presently accepted under the designation of lichen myxedematosus. This entity includes skin findings other than papules, but one can create additional subdivisions in the above subgroup to describe the particular nature of those lesions showing other morphological changes.

THEORIES ON ETIOLOGY OF LOCALIZED MYXEDEMA

Several investigators [18] developed a circulatory stasis theory based on cardiac failure to explain the pretibial type of myxedema. Pillsbury and Stokes [8] proposed local trauma as an additional inciting factor in these cases. Some workers [19] postu-

TABLE 1.—*Mucinoses (Myxedema; Solid Edema)*

I. Universal (Generalized; Diffuse)		II. Localized (Circumscribed)	III. Neoplasms
A. Clinical	B. Subclinical	See Table 2.	A. Sarcomata
1878 Ord [2]	1931 Reuter [4]		B. Lipomata
Generalized myxedema of hypothyroidism	Showing only lowered basal metabolic rate		C. Fibromata

TABLE 2.—*Circumscribed (Localized) Types of Mucinoses*

A. With Hyperthyroidism	B. No Demonstrable Thyroid Disease	C. With Hypothyroidism
1889 Morrow [6] Symmetrical areas of solid edema occurring in Graves's disease	1935 Neumann [11] Mucoid papular disease	1916 Dössekker [3] Tuberous myxedema
1930 O'Leary [7] Localized solid edema	1935 Neumann [11] Lichen myxedematosus	
1931 Pillsbury and Stokes [8] Circumscribed myxedema	1941 Dalton [12] Generalized localized myxedema	
1942 Trotter and Eden [9] Circumscribed pretibial myxedema	1951 Lorincz [13] Lichen fibromucinoidosis	
1946 Cohen [10] Myxoedema circumscriptum thyrotoxicum	1952 Dalton and Seidell Papular mucinosis	

lated a theory of "local hypothyroidism" in the skin, and others [20] suggested a state of hypothyroidism underlying a "dysthyroidism." Various writers have interpreted both pretibial and nonpretibial forms of myxedema as instances of thyroid dysfunction. However, Scheuermann [17c] regarded those cases with hypothyroidism which responded to thyroid administration as having merely local deposits of mucin instead of a diffuse distribution.

18. (*a*) Richter, W.: Über lokales Myxödem der Haut, mit Beziehung zum Basedow, Dermat. Wchnschr. **84**:51, 1927. (*b*) Pillsbury and Stokes.[8] (c) Arzt, L.: Zur Frage des lokalen Myxödem bei Basedow, Med. Klin. **30**:49-52, 1934.

19. (*a*) Urbach, E.: Endokrin bedingte Haut- Schleimhaut- und Haarerkrankungen, Arch. Dermat. u. Syph. **161**:492-503, 1930. (*b*) Marchionini, A., and Jahn, D.: Elephantiastisches tuberöses Myxoedema circumscriptum bei Morbus Basedow: Ein Beitrag zur Endokrinopathologie der Haut, Arch. Dermat. u. Syph. **176**:694-704, 1938. Carol.[17b] Richter.[18a]

20. (*a*) Keining, E.: Myxoedema circumscriptum symmetricum maessigen Grades bei Basedow, Dermat. Wchnschr. **87**:1874-1875, 1928. (*b*) Pillsbury and Stokes.[8]

Trotter and Eden[9] (1942) concluded, "There is no good reason for supposing that the lesions of localized pretibial myxedema are in any sense the result of hypothyroidism." They hypothesized that pituitary overactivity might be the underlying common etiology for mucin deposition in both hyperthyroidism and hypothyroidism. Following this pituitary-thyroid axis concept, Curtis, Cawley, and Johnwick[21] (1949) reasoned that localized myxedema and progressive exophthalmos are allied manifestations of the same disorder and are probably due to an excess of the thyroid-stimulating hormone. They cite Plummer and Wilder's[22] (1934) reference to the overfunction of the anterior pituitary as a possible cause for exophthalmos.

Duran-Reynals[23] proposed that the morbid changes in myxedema occur in the intercellular material or "ground substance" of the connective tissue. This material is now known to contain several mucopolysaccharides, among which are hyaluronic and chondroitin sulfuric acids.[24] Current data suggest that the concentration of the enzyme hyaluronidase, which may possibly occur in the skin, may be a factor in determining the amount, state, and composition of the intercellular substance.[25]

An unexpressed conception of the theory of such an enzyme-substrate relationship in the connective tissue was possibly embodied in Trotter and Eden's[9] suggestion to inject hyaluronidase into patches of localized myxedema. This procedure was carried out by Grais,[26] with a regression of such lesions. Thus, the identification of "spreading factors," hyaluronidase and possible antihyaluronidase, opens a new field for further investigation of myxedema.

Von Fischer[27] proposed a defect in the ability of the liver to synthesize albumin as the cause of this disease. This was based on the electrophoretic findings of decreased albumin and increased beta and gamma globulin in the serum in his case of myxoedema tuberosum. Since one of our patients showed a similar pattern, his theory seems worthy of further investigation.

REPORT OF CASES

Dr. C. C. Barrett,[28] of Lexington, Ky., presented the following case for diagnosis at the May, 1940, meeting of the Cincinnati Dermatological Society. Since the proceedings of that Society are not published, he permits us to officially record this case here.

---

21. Curtis, A. C.; Cawley, E. P., and Johnwick, E. B.: Association of Progressive (Malignant) Exophthalmos and Localized Myxedema, Arch. Dermat. & Syph. **60**:318-337, 1949.

22. Plummer, W. A., and Wilder, R. M.: Etiology of Exophthalmos: Constitutional Factors with Particular Reference to Exophthalmic Goiter, Tr. Am. Acad. Ophth. **39**:41, 1934; Arch. Ophth. **13**:833-852, 1935.

23. Duran-Reynals, F.: The Ground Substance of the Mesenchyme and Hyaluronidase: Introduction, Ann. New York Acad. Sc. **52**:946-956, 1950.

24. Meyer, K., and Palmer, J. W.: The Polysaccharide of the Vitreous Humor, J. Biol. Chem. **107**:629-634, 1934.

25. McMaster, P. D., and Parsons, R. J.: The Movement of Substances and the State of the Fluid in Intradermal Tissue, Ann. New York Acad. Sc. **52**:992-1003, 1950.

26. Grais, M.: Local Injections of a Preparation of Hyaluronidase in the Treatment of Localized (Pretibial) Myxedema, J. Invest. Dermat. **12**:339-343, 1949.

27. von Fischer, F.: Beitrag zur Klinik und Pathogenese des Myxoedema tuberosum, Dermatologica **98**:270-288, 1949.

28. Barrett, C. C.: Personal communication to the authors.

CASE 1.—*History.*—In mid-April, 1940, a 63-year-old, white, married laborer was seen because of an asymptomatic skin complaint. This eruption began in 1937 about the extensor surfaces of both forearms. It gradually spread in those locations and appeared at distant points. No other noteworthy illness accompanied, preceded, or followed the onset of this complaint.

Cutaneous Examination.—The early lesions appeared as asymptomatic, shiny, wax-like, moderately elevated, rounded, flat-topped papules, 2 to 6 mm. in diameter. Some of the older ones developed fine scaling. These elements appeared singly, but had a marked tendency to group into solid patches in which individual papular outlines were retained. The edges of the patches were usually sharply demarcated but sometimes feathered out at the periphery. The eruption was strikingly symmetrical. It was distributed about the forehead, glabella, chin, ear lobes, shoulders, scapulae, upper arms, elbows, forearms, knees, and the lateral surfaces of the lower legs. It predominated on the extensor surfaces but occurred to a lesser degree on the flexor surfaces of the upper extremities. On movement, there was a sense of stiffness in the patches overlying joints, but there was no evidence of scleroderma-like changes.

The uninvolved skin was of normal color and presented the usual drying, wrinkling, and thinning that would be expected in a man of his age. The hair showed graying, coarsening, and thinning in the crown area. The patient was edentulous. The nails were work thickened. The accessible mucous membranes were moderately pale.

General Examination.—The patient seemed physically well preserved, unworried, normally alert, and vigorous for his age. He was of medium height and of linear build, with good residual muscular development. Inspection of the genitalia and other external areas was unrevealing. The blood pressure, pulse, and respiratory rates were normal. Physical examination revealed no changes in internal organs.

Histopathological Examination.—Two biopsy specimens were taken from affected skin areas and sent to Drs. Fred Weidman and Hamilton Montgomery in early May, 1940. Both made a diagnosis of myxedema. Dr. Weidman made special note of the finding of densely packed, blue, mucinous granules within the secretory cells of the sweat glands. Though the granules were located in all parts of these cells, they were more numerous about the lumen. Furthermore, he observed that the involuntary muscle around the sweat coils was thickened. He suggested that mucin was possibly undergoing excretion through cells of the sweat glands.

Other Studies.—The patient died in late May, 1940. Death came suddenly in his home, and it was impossible to ascertain the exact cause. Thus, other studies could not be done.

CASE 2.—*History.*—This previously published case [12] is that of a white, obese, twice-married woman, who was first seen by one of us (J. E. D.) on Oct. 31, 1939, when she was 24 years old. She was 37 years old at the time of this report. In addition to her household duties, she has worked as a grocery clerk, a taxi driver, and a waitress.

Her initial complaints of skin eruption, menstrual disturbance, growing frigidity, and increasing weight appeared simultaneously in February, 1938, following a severe attack of influenza.

The skin eruption began as small, elevated, yellowish, asymptomatic lesions about the extensor surfaces of both elbows and the adjacent parts of both upper and lower arms. It remained static until March, 1939, when newly developing lesions coalesced with the older ones to form patches at the primary sites, and scattered papules appeared over all surfaces of both forearms. Four months later, a cluster of such lesions appeared at the glabella, simultaneously with an eruption on both lower legs. Gradually these skin changes became widespread. Recently, questionable lesions were noted on the buccal mucosae and the inner surfaces of the labia minora. There has never been any scleroderma-like facies, sclerodactylia, or Raynaud's phenomenon, as described in some of the other cases.

Between 1933 and 1938 she had two pregnancies. One terminated at the sixth and the other at the second month in unexplained miscarriages. Early in 1938 her normal menses became unpredictable in cycle, lessened in flow, and associated with cramping. An associated frigidity developed and has increased. Between 1938 and 1940 periods of amenorrhea alternated irregularly with others of hypomenorrhea, and in mid-1940 her menses ceased. A constant scanty white discharge followed, and the persistent pelvic pain increased. On Nov. 25, 1940, both ovaries, both tubes, the uterus, and the appendix were removed, with resulting freedom from pelvic

symptoms. The original diagnosis, made elsewhere on the surgically removed material, was periappendicitis and papillary cystadenoma of a cystic ovary. When the material was restudied here, a report of pseudomucinous cystadenoma of the ovary with probable low-grade malignancy was made.

The patient's normal weight of 128 lb. (58 kg.) increased abruptly to 200 lb. (91 kg.) between February, 1938, and October, 1939. On a strict diet, irrespective of the various endocrine preparations therapeutically tried, her weight fell to 161 lb. (73 kg.), but it increased again on a return to unrestricted food intake. Following surgery, the weight reached 220 lb. (100 kg.), but was reduced to 200 lb., the last reported weight, by diet alone. There has been some questionable improvement in the eruption whenever her weight decreased.

Thorough histories dealing with past illnesses, diet and other systems were unrevealing, and she has maintained good general health.

Fig. 1.—Papular lesions of left forehead, brow, glabella, nose angle, lower lip, chin, submental area and side of neck.

Therapeutic trial was made of thyroid, estrone (theelin), a gonadotropin preparation obtained from the urine of pregnant mares (gonadogen®), an anterior pituitary growth hormone preparation (polyansyn®), diethylstilbestrol, octofollin, and vitamin C. The last gave questionable skin improvement, but the others had no effect. On the basis of von Fischer's [27] report, the patient was started on 15 grains (0.97 gm.) of theobromine calcium salicylate (theocalcin,® Bilhuber-Knoll), given orally after meals, but no beneficial result was obtained.

Cutaneous Examination.—The newest skin lesions appeared as yellowish, shiny, domed, rounded papules, 1 to 5 mm. in diameter. They occurred singly, in annuli, and in lines. The latter were sometimes grouped along preexisting striae. The older lesions had taken on a dull pinkish color, and the adjacent papules tended to coalesce into patches in which the individual outlines were retained. The eruption was distributed in a roughly symmetrical manner about the forehead, brows, glabella, lips, nose angles, chin, temples, ear rims, cheeks, sides of neck, submental area, shoulder apices, anterior and posterior axillary folds, upper arms, elbows, lower arms, wrists, dorsa of hands and fingers, abdomen, buttocks, thighs, knees, lower legs, and dorsa of the feet (Figs. 1, 2, 3, and 4). Lately questionable lesions have been noted on the buccal mucosa and the inner surfaces of the labia minora, but a biopsy of these failed to show significant changes. Some of the linear lesions exhibited a beading with individual papules which clinically

Fig. 2.—Papular lesions occurring singly and in patches about right shoulder apex, upper arm, elbow, forearm, wrist and dorsum of hand and fingers.

Fig. 3.—Distribution of eruption over right buttock, thigh, knee, lower leg, and ankle. Lesions of dorsum of foot not shown in photograph.

suggested lichen ruber moniliformis.[29] Lesions were absent in vaccination and surgical scars and on the palms, soles, scalp, chest, and back. They predominated on extensor surfaces but were present to a lesser degree in flexor areas.

The earlier tendency for papules to form solid patches has changed to a greater inclination for them to group into annuli. Although but few lesions have spontaneously disappeared, a regression of papules has regularly occurred in the zone immediately surrounding the site of each biopsy (Fig. 4).

Fig. 4.—Photograph taken in 1940 showing single, annular, linear, and patch arrangements of symmetrical eruption over posterior portion of thighs, knees, and lower legs. Note zone of clearing surrounding site of biopsy in patch involving mid-latero-posterior portion of left lower leg.

The uninvolved skin was normal in color, texture, and moisture. The hair showed no change in its amount, structure, or distribution. The nails and teeth were unaltered. Accessible mucous membranes showed no definite changes.

General Examination.—The patient appeared as a normally voiced, intelligent, alert, relaxed, energetic, active, happy, strong, obese individual. She was of medium height, and her body build

29. Wise, F., and Rein, C. R.: Lichen Ruber Moniliformis (Morbus Moniliformis Lichenoides): Report of a Case and Description of a Hitherto Unrecorded Histologic Structure, Arch. Dermat. & Syph. **34**:830-849, 1936.

was square, with a broadness of the face and hands and wide flatness of the feet. There was some tendency for fat to be more prominently distributed about the hips. The breasts were flat, but no atrophy of the labiae, vagina, or uterus existed. Blood pressures ranged from 110 to 130 systolic and from 60 to 80 diastolic. The pulse and respiratory rates and body temperatures have repeatedly been normal. External and internal examination of the eyes and visual fields showed no pertinent findings. All reflexes were normal. Repeated physical examinations have been unrevealing.

Special consultation with internists, endocrinologists, an ophthalmologist, an otolaryngologist, a gynecologist, and a surgeon, and with other dermatologists has failed to contribute additional findings.[30]

Histopathological and Histochemical Studies.[31]—Early the histopathological diagnosis of myxedema was independently rendered by Drs. Hamilton Montgomery and Fred Weidman, and others have since concurred in this. Drs. Zola Cooper and A. I. Lansing are responsible for carrying out the techniques of the histochemical studies.

Three biopsies of the affected skin were made in 1939, two in 1944, and four in 1951. For comparison, specimens were taken from the uninvolved skin and the zone of postbiopsy clearing. Bouin's fluid, 10% formalin, lead acetate, alcohol-formalin solution, and 50% alcohol were used as fixatives. All the biopsy specimens from the involved skin exhibited essentially identical pictures. In a hematoxylin-stained section through one of the papules, the epidermis showed slight hyperkeratosis but was otherwise essentially normal. The rete ridges were obliterated, probably because of pressure from the dermal lesion. Pigment in the basal layer was conspicuous. There were clearly delimited areas in the upper dermis in which the fine collagen fibers had a loose and disorderly arrangement. One examiner (F. W.) in one biopsy placed this at the level of the subpapillary plexus of blood vessels. Here, individual collagen fibers seemed to be separated from one another by spaces in which there was basophilic fibrillar material (Fig. 5, *A* and *B*.). Elongated and stellate cells were present which resembled embryonic connective tissue cells (Fig. 5*C*). Collagen fibers in the lower dermis were essentially normal in size and arrangement. Throughout the dermis, blood vessel walls were somewhat thickened and a moderate perivascular infiltrate of lymphocytes and histiocytes was present. Mast cells were present in normal numbers (Fig. 5*B*).

Sections stained for fats and for amyloid were negative. Iron stain on others showed some deposit of iron around blood vessels (H. M.).

In sections stained with mucicarmine (Fig. 5*D*), the areas of disorderly arrangement of fibers in the upper dermis were found to contain mucin. This substance was in the form of fine granular and fibrillar material between the collagen bundles. A Masson trichrome stain for collagen and a Verhoeff stain for elastic tissue showed these two types of fibers to be essentially unchanged in their staining reaction and distribution. They seemed merely to be separated by the mucinous material, so that the affected areas when stained with either stain had a loose reticular appearance. On repeated trials in two different laboratories (A. L. and Z. C.), reticulum fibers could not be stained in these areas by Wilder's method. However, the reticulum about blood vessels

30. Clinical aid was given by Dr. W. A. Dinninger (Winchester, Ind.); Drs. Brandt Steele and Donald Pillsbury (Philadelphia); Drs. J. O. Ritchey, Kenneth Kohlstaedt, C. L. Rudesill, Marlow Manion, D. C. Hines, J. J. Mahoney, Frank Rabb, and J. W. Hofmann (Indianapolis); Drs. Paul O'Leary and Hamilton Montgomery (Rochester); Drs. Clinton Lane, Richard Weiss, Martin Engman Jr., and Louis Cohen (St. Louis); Drs. F. E. Senear and Marcus Caro (Chicago); Dr. Wiley Sams (Miami); Dr. Everett Seale (Houston); Dr. D. C. Smith, (Charlottesville, Va.); and the Cincinnati, Central States, and Mississippi Valley Dermatological Societies.

31. Histopathological and histochemical aid was given by Drs. Hamilton Montgomery (Rochester); Fred Weidman (Philadelphia); C. G. Culbertson and J. L. Arbogast (Indianapolis); Marcus Caro (Chicago); Elson Helwig (Washington), and A. I. Lansing and Zola K. Cooper (St. Louis).

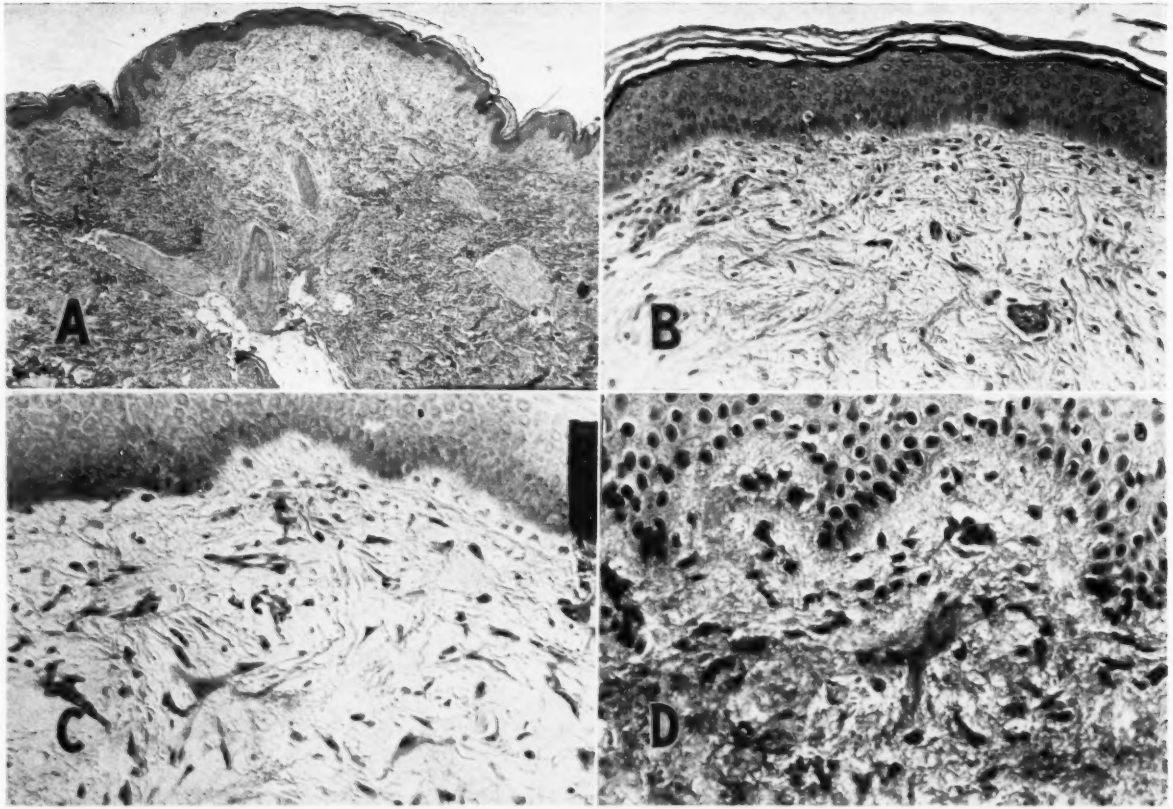


Fig. 5.—*A*, low-power photomicrograph showing papular lesion in upper dermis; hematoxylin and eosin stain; × 25. *B*, portion of lesion shown in *A* under higher magnification to show loose and disorderly arrangement of collagen fibers of dermis which are separated from one another by spaces; hematoxylin and eosin stain; × 120. *C*, stellate and elongated cells in lesion in upper dermis, which resemble embryonic connective-tissue cells; methylene blue stain. *D*, portion of lesion in upper dermis showing deposition of finely granular mucinous material between collagen bundles, mucicarmine stain; × 120.

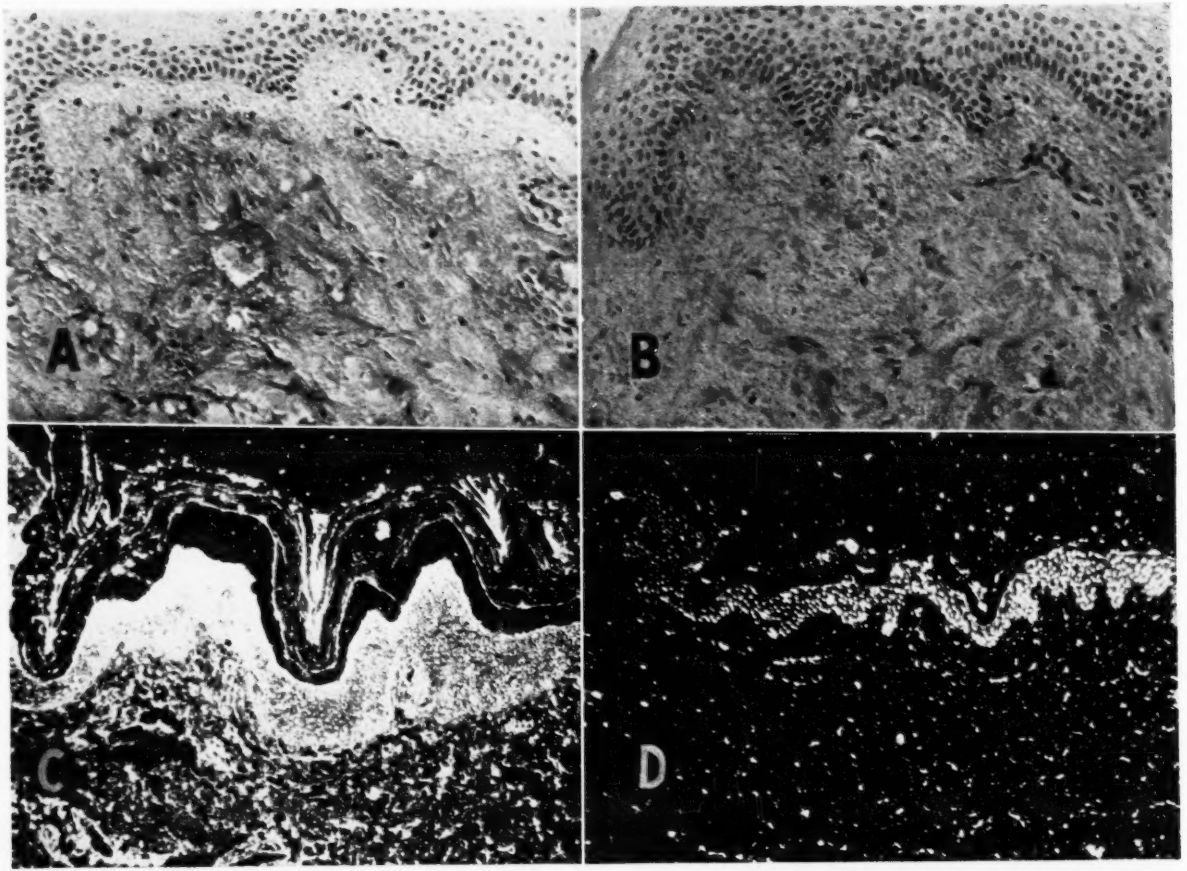


Fig. 6.—*A*, portion of lesion in upper dermis showing metachromatic material between collagen bundles; toluidine blue stain. *B*, same portion of lesion as in *A* after digestion of section with hyaluronidase. Metachromatic material has disappeared, indicating that it has a high hyaluronic acid content. *C*, microincinerated section of portion of lesion showing clumps and fine granules of white ash (calcium and magnesium oxides) in areas which by other methods had been shown to contain mucinous material. *D*, microincinerated section of patient's uninvolved skin showing very little white ash in upper dermis.

in the same slide stained clearly. Also control sections of spleen, stained at the same time, showed the normal pattern of reticulum. Furthermore, reticulum could not be clearly shown in the uninvolved skin or in the zones of postbiopsy clearing.

Tissue from the involved and the uninvolved areas, and from zones of postbiopsy clearing fixed in lead acetate and also in alcohol-formol solution, were stained by the periodic acid-Schiff technique (Hotchkiss-McManus). Control slides were stained with the Schiff reagent for comparison. With the Schiff reagent all the biopsy specimens stained a pale pink, with no concentration of the red coloration which indicates a lack of free aldehydes. A periodic acid-Schiff reaction showed a dense red color in the walls of blood vessels and in the basement membrane of the epidermis, and diffuse red coloration in the papular lesions in the upper dermis. The diffuse rather than the selective stain with paraaminosalicylic acid corresponded to the lack of silver impregnation for reticulum in the lesions.

In an attempt to determine more about the nature of the mucinous material in the upper dermis, some sections were stained with thionine and others with toluidine blue. With both stains this material was metachromatic.

Since all these procedures indicated the presence of mucopolysaccharides in the papular lesions in the upper dermis, studies were carried out to determine the effect of hyaluronidase on this material. Biopsy specimens were taken from an area of involved skin, from uninvolved skin, and from a zone of postbiopsy clearing. All were fixed in lead acetate, and paraffin sections were prepared. One slide from each specimen was incubated at room temperature for 18 hours in a solution of hyaluronidase (Schering) containing 3 turbidity reducing units per cubic centimeter. These slides and undigested control slides from each specimen were then stained in 0.5% aqueous solution of toluidine blue, washed in tertiary butyl alcohol, dehydrated, cleared, and mounted.

The undigested sections of involved skin (Fig. 6*A*) showed metachromatic material in the papular lesions in the upper dermis but duplicate sections digested with hyaluronidase (Fig. 6*B*) showed a complete absence of metachromasia. The uninvolved skin showed only the very faint trace of metachromasia that would be expected in normal skin. After incubation with the enzyme, this faint coloration disappeared. Sections prepared from the zone of postbiopsy clearing showed no metachromasia either before or after incubation with hyaluronidase.

From these observations it was determined that the mucopolysaccharides present in the involved skin were digestible in hyaluronidase and therefore probably had a high hyaluronic acid content. The uninvolved skin and the zone of postbiopsy clearing did not contain significant amounts of this material.

A single biopsy specimen, which included involved skin and some of the surrounding uninvolved skin, was fixed in acidified silver nitrate in alcohol in an attempt to study ascorbic acid in the tissue. This method is based on the fact that vitamin C reduces acidified silver nitrate. Fine black granular material was found in the mid-dermis in the lesion and not in the unaffected skin. On the basis of this single biopsy, there would seem to be an increase in ascorbic acid in the affected skin. No definite conclusions could be drawn from so limited a study.

Other pieces of skin from the involved areas, the uninvolved areas, and the zones of postbiopsy clearing were fixed in alcohol-formol solution (9 parts absolute alcohol and 1 part 40% dilution of formalin) and paraffin sections were prepared. These sections were then incinerated in a quartz tube oven at 500 C. for 30 minutes. The ashed sections of the involved skin showed clumps and fine granules of white ash in the upper dermis in the areas which by other methods had been shown to contain mucinous material (Fig. 6*C*). The zones of postbiopsy clearing also contained white ash in the upper part of the dermis, but here the ash was more finely divided and less in amount than in the involved skin. The uninvolved skin (Fig. 6*D*) showed very little white ash in the upper dermis. The bulk of white ash in microincinerated sections was generally conceded to be made up of calcium and magnesium oxides.

Roentgenological Studies.[32]—Repeated x-rays of chest, heart, humeri, femora, and skull were negative. Careful examination of the sella turcica was unrevealing, and no substernal thyroid was demonstrable.

Clinical Laboratory Studies.[33]—Skin Procedures: Intradermal Congo red and tuberculin tests were negative. Studies of capillary fragility and of cold pressor reaction were unrevealing. Clearing of the papules adjacent to a biopsy site was observed regularly. Regression of skin lesions also followed the application of liquid phenol and neutralization with water; a moderate time-pressure exposure to solid carbon dioxide, and mild curettage, and the intradermal injection of high dosages of hyaluronidase, followed by prolonged pressure.

Urine Procedures: Results of numerous complete urinalyses were negative. Rechecked studies of 17-ketosteroids and 11-oxysteroids gave normal values. Repeated assays for estrogen showed only a questionable adrenal hyperfunction and those for gonadotropic hormone were normal for a castrate.

Blood Procedures: Repeated blood cell counts, hematocrit readings, and hemoglobin and coagulation-time determinations gave normal results.

Two standard glucose tolerance tests, an Exton-Rose test, and an insulin tolerance test gave somewhat elevated curves, but other standard tests and an intravenous glucose tolerance test showed normal values. Results of the carbon-dioxide-combining power and a diastase (amylase) test were normal.

Several determinations of total proteins, albumin, globulin, total nonprotein nitrogen, urea nitrogen, creatinine, uric acid, and mucoproteins showed normal values. A rechecked electrophoresis of serum showed a decrease of 14% in albumin and an increase of 14% in gamma globulin.

Three total lipid studies showed elevation (1,770, 1,070, and 1,036 mg. per 100 cc.), whereas two others showed normal values (528 and 530 mg. per 100 cc.). In a series of six cholesterol studies, two showed elevation (263 and 275 mg. per 100 cc.). Rechecked determinations of both the cholesterol esters and lecithin showed elevation in one test (cholesterol esters 190 mg. and lecithin 258.7 per 100 cc.) and normal values in the other.

A liver profile, including bilirubin, sulfobromophthalein alkaline phosphatase, acid phosphatase, cephalin flocculation, and thymol turbidity tests, was essentially normal. Rechecked studies of serum chlorides (as Cl), sodium, potassium, and calcium, and of phosphorus gave normal values. Results of repeated serologic tests, a complement fixation for gonococci, a cold agglutinin test, and an eosinophile count before and after a subcutaneous injection of epinephrine gave normal results. An ascorbic acid assay of buffy coat gave a lowered value (0.4 mEq. per cubic centimeter), and a protein-bound iodine determination was below normal (3.0 mEq. per 100 cc.).

Miscellaneous Procedures: A cervical culture and a stool examination were negative. A series of six basal metabolic rates ranged from —9% to +13%. Two electrocardiograms were normal, and a blood pressure series ranged from 110 to 130 systolic and 60 to 80 diastolic.

COMMENT AND SUMMATION OF FINDINGS IN CASES

Histopathological and Histochemical Studies.—The lesions seemed to consist of mucinous material deposited between essentially normal collagen and elastic tissue fibers in the upper dermis. In these areas stellate and elongated cells were present which resembled the cells found in embryonic connective tissue, but reticulum fibers could not be demonstrated.

---

32. Roentgenologic aid was given by Dr. Bruce Stocking (Muncie, Ind.); Indiana University and Indianapolis General Hospitals (Indianapolis); and Jewish Hospital (St. Louis).

33. Clinical laboratory aid was given by Drs. C. G. Culbertson, J. L. Arbogast, William Drake, Kenneth Kohlstaedt, W. W. Davis, S. M. Zwingle, J. J. Mahoney, and R. L. Dryer (Indianapolis); Dr. Lall Montgomery (Muncie, Ind.); Barnard, Barnes, and Jewish Hospitals (St. Louis); and University of Minnesota School of Medicine. Lyophilized hyaluronidase (wydase®) was supplied for the injection studies by Dr. E. Farrar Jr., of Wyeth, Inc., Philadelphia 2, Pa.

The mucinous material was metachromatic, and this indicated that it was a mucopolysaccharide. This material was digested by hyaluronidase which points to the fact that it contained hyaluronic acid. It was not present in uninvolved skin or in zones of postbiopsy clearing.

The failure to stain reticulum both by paraaminosalicylic acid and by silver impregnation in either the involved or the uninvolved skin of this patient suggested that there might be a fundamental defect in the formation of white fibrous connective tissues. Way [34] also reported the absence of reticulum fibers in myxedema as well as in certain other cutaneous diseases.

By microincineration studies, the lesions were shown to be areas of hypermineralization, and the ash present was either calcium or magnesium or both.

The Clearing Phenomenon.—The "clearing phenomenon" observed in those papules immediately surrounding the site of each biopsy led one of us (J. E. D.) in 1942 to attempt to reproduce a like picture by other methods. Thus, it was found that a similar regression could be accomplished by the application of liquid phenol followed shortly by water neutralization and by a moderate time-pressure exposure to dry ice followed by mild curettage. Attempts to attain this by procaine injections or by dry ice applications alone failed. Grais [26] also noted that the incision of a patch of pretibial myxedema led to a two-week-long mucinous drainage, which was followed by a return to "essentially normal skin." Further studies on this clearing phenomenon are in progress and will subsequently be reported.

Hyaluronidase Studies in Vivo.—Local hyaluronidase injections into patches of pretibial myxedema were originally proposed by Trotter and Eden.[9] Such a procedure was carried out by Bloom, Herrmann, and Sharlit,[35] by Grais [26] and others, and all reported regression of lesions. However, there are no reports in the literature on the injection of hyaluronidase into lesions of lichen myxedematosus. In Case 2 intradermal injections of this enzyme produced clearing, if the dosage was sufficiently high and if prolonged constant pressure was maintained over the site of introduction. Thus, these in vivo studies paralleled the clearing observed in the histochemical studies on tissue sections.

Endocrinological Studies.—No clear-cut endocrinopathy could be established from the clinical and laboratory studies on Case 2. The clinical complaints of menstrual disturbance, frigidity, and obesity suggested some endocrinological disturbance. However, the pseudomucinous cystadenoma of the ovary, which was found at surgery, probably explains the gradual cessation of menses and the loss of libido. The obesity seemed to be of exogenous origin, inasmuch as weight could be reduced and held down by diet alone.

In respect to the assays on urine, no specific picture was found. A consulting endocrinologist (Mahoney) stated, "With the existing surgical absence of ovaries and if aberrant ovarian tissue is not present, the estrogen assay findings may mean a questionable adrenal hyperfunction. The gonadotropic assay reports present the normal levels for a castrate." However, a subcutaneous epinephrine test with study of the eosinophiles failed to reveal an adrenal abnormality.

---

34. Way, S. C.: Reticulum, or Lattice, Fibers, Arch. Dermat. & Syph. **55**:478-492, 1947.

35. Bloom, D.; Herrmann, F. J., and Sharlit, H.: Local Injections of a Preparation of Hyaluronidase in the Treatment of Mucinous Infiltration of the Skin, J. Invest. Dermat. **12**:339-343, 1949.

The test for protein-bound iodine in blood gave reduced values. However, most workers in that field mention the present complexities in the method and the difficulty in evaluating iodine studies on blood. Thus, in the absence of other confirmatory clinical or laboratory evidences of thyroid disease, we cannot put much emphasis on this single finding.

The first standard glucose tolerance test and a later Exton-Rose test showed upper borderline readings, but a second standard test and insulin tolerance study gave essentially normal curves. A consulting internist, who specializes in diabetic diseases (Rudesill), was unwilling to class these laboratory reports as indicating any abnormality when they were reviewed with the patient's complete picture. He proposed that an intravenous glucose tolerance test be done. This was carried out, and the report showed normal ranges.

Lipid Studies.—Lipid studies were noncontributory. The first report of elevated total lipids was admitted to be a probable laboratory inaccuracy, but the rechecked increase, which was found on March 10, 1950, is hard to appraise in the presence of normal levels shown on both May 3 and June 25, 1940.

Reports on cholesterol values are notorious for their variability. Therefore the two elevations, which occurred in a series of otherwise normal tests, were disregarded.

The slightly elevated readings on one occasion each for cholesterol esters and for lecithin determinations are likewise probably of no consequence. However, the cholesterol ester levels are consistently high enough to suggest the absence of hepatic dysfunction.

Liver Function Studies.—No conclusive evidence of a liver dysfunction could be demonstrated. Electrophoretic studies on serum in von Fischer's[27] case showed a hypoalbuminemia with increased beta and gamma globulin, and a similar pattern was found in two such separate tests in Case 2. However, a complete liver profile done on our patient failed to explain these abnormalities. Furthermore, her blood albumin-globulin ratio was repeatedly unchanged and the serum mucoproteins, which have been regarded as alpha′ globulin, were found normal in two different laboratories by the same tyrosine method.

A punch biopsy of the liver was considered. However, if lichen myxedematosus is associated with liver disease, it would probably involve a function rather than a morphological change, and a liver biopsy would probably not contribute enough to warrant subjecting the patient to this procedure.

CONCLUSION

In conclusion, we offer no specific etiology for lichen myxedematosus. The isolated facts found in this report may aid someone in a later study. Probably the eventual explanation of this entity will be found in some factor or factors acting locally in the skin.

ABSTRACT OF DISCUSSION

DR. H. N. COLE, Cleveland: Various terms have been suggested for this entity. Dubreuilh[14] called it *fibromes miliaires folliculaires, sclerodèrme consécutive.* Dössekker[3] described it as tuberous myxedema. Per and Rossiansky used the same term (Per, M. I., and Rossiansky, N. L.: *Arch. Dermat. u. Syph.* **156**:320, 1928). Pellizarri speaks of it as myxomatosus nodosa (*Arch. Dermat. u. Syph.* **112**:7, 1912). Ormsby, Montgomery, and Sutton used the term circumscribed myxedema. Neumann's term was mucoid papular disease. The name employed in 1899 by one

of our deceased members, Howard Morrow,[6] then studying in London, was solid edema occurring in Graves's disease. Dr. Dalton suggests the term papular mucinosis. It has its advantages, except that of long usage. He has been most fortunate in having in his second case one of the most extensive involvements of the skin thus far reported in the literature.

The extensive investigation he has been able to carry on adds to our knowledge of the disease. Thus a biopsy may cause a zone of clearing. O'Leary[7] also noted this, with keloid formation after excision of a plaque. Was it the keloid or the biopsy? An application of phenol neutralized in 60 seconds did the same; a 45-second application of solid carbon dioxide produced no change unless there was added curettage.

Local injection into lesions of the spreading agent hyaluronidase along with a pressure bandage produced local regression. Without the added pressure no change was noted.

Generally, thyroid extract has not helped or even accentuated the process. However, in the first case of Pillsbury and Stokes,[8] and in that of Morrow[6] there was great benefit for a time. Goldenberg's patient (Case Presentation, *J. Cutan. Dis.* **34**:387, 1916) was greatly benefited. The effect would indeed depend upon the condition in the particular patient.

Grynkewich, Herron, and others (*Am. J. M. Sc.* **222**:142, 1951) think that myxedema never occurs in the absence of exophthalmos; yet Netherton in his discussion of the paper of Curtis, Cawley and Johnwick,[21] reported that in a review of 13 cases of localized myxedema at the Cleveland Clinic, only 7 of 13 had an associated exophthalmos. In Dr. Dalton's second case, apparently the thyroid played no great role. The patient's basal metabolic rate was always around the normal or a little low. There were other glands of internal secretion that were affected in this case, and a review of the literature seems to show a rather general feeling that in this disease there may be a multiple involvement of glands rather than that of the thyroid alone. How often in these cases one notes an associated diabetes.

In Dössekker's case, that of a Swiss chamois hunter, Prof. Theodore Kocher twice took a part of a thyroid gland from a patient with Graves's disease and implanted it into the bone marrow, first in one shin bone and one month later in the other. The patient recovered completely, even though he had had large mulberry masses over the scrotum and extensive nodular masses over the forehead, head, ears, chest, and upper back.

Per and Rossiansky's patient, a man aged 42, likewise had the circumscribed nodular masses over the forehead, scalp, right cheek, neck, trunk, and upper extremities. Professor Golzanitsky removed material from a hypertrophied colloid goiter and implanted part of this in the muscles of the breast, and of the remainder he made an emulsion and injected 10 cc. into the large tumor on the forehead and several others. A month later the procedure was repeated. All the tumors, and especially the ones into which the injections had been made, became smaller, and 12 disappeared entirely.

The last word has yet to be said on tuberous myxedema or papular mucinosis. Undoubtedly the condition is bound up with the glands of internal secretion, and not always the thyroid alone.

DR. J. E. DALTON, Indianapolis: I am honored to have had this paper discussed by Dr. Cole, who directed my major training. Furthermore, I am indebted to Dr. Barrett, who was my senior on residency for his permission to include his case in this study. Thus, this day revives many of my earlier pleasant associations.

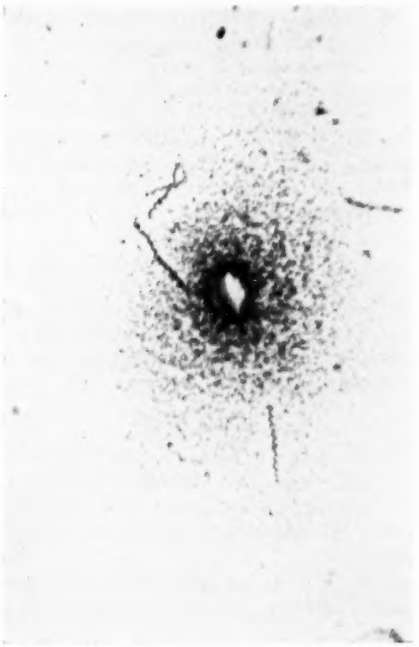
I should like to reemphasize the point that lichen myxedematosus is not associated with any demonstrable thyroid disease and that this fact definitely separates these cases from other forms of localized myxedema.

Clinical Notes, New Instruments and Techniques

RAPID AND EASY METHOD FOR STAINING SPIROCHETES WITH FOUNTAIN PEN INK

EDWARD T. EMURA, M.D.
CINCINNATI

THERE are two major techniques for staining spirochetes.[1] One consists of impregnating the spirochetes with a dye or metallic ion and rendering it visible against a light background, e. g., by use of silver impregnation and carbol-methyl-violet stain.[2] The other consists of rendering the unstained spirochetes visible by making the background black with staining, e. g., by using India ink preparations.



Treponema pallidum from Case 11 stained with Parker 51 blue-black ink.

From the Department of Dermatology and Syphilology of the College of Medicine of the University of Cincinnati, Director, Dr. Leon Goldman.

1. Campbell, R. E., and Rosahn, P. D.: Morphology and Staining Characteristics of Treponema Pallidum: Review of Literature and Description of New Technique for Staining the Organism in Tissues, Yale J. Biol. & Med. **22**:527-543 (July) 1950.

2. De Lamater, E. D.; Haanes, M., and Wiggal, R. H.: Studies on Life Cycles of Spirochetes: II. Development of New Stain, Am. J. Syph. **34**:515-518 (Nov.) 1950.

Correlation of Results of Examination with Dark-Field and Ink-Stain Methods

Patient	Diagnosis	Dark-Field	Parker 51
1	Primary syphilis	+	+
2	Primary syphilis	+	+
3	Secondary syphilis, late	—	—
4	Secondary syphilis, late	—	—
5	Secondary syphilis, late	—	—
6	Reinfection, early	+	+
7	Varicella, pustular syphilis ruled out	—	—
8	Primary syphilis, ruled out	—	—
9	Relapse syphilis, ruled out	—	—
10	Chancroid, syphilis ruled out	—	—
11	Secondary syphilis, early	+	+
12	Secondary syphilis, late	—	—
13	Chancroid, syphilis ruled out	—	—
14	Chancroid, syphilis ruled out	—	—
15	Primary syphilis	+	+
16	Herpes progenitales?	—	—
17	Primary syphilis	±	+
18	Chancroid?	—	—
19	Primary syphilis	+	+
20	Primary syphilis, Kahn-positive	—	+
21	Chancroid?	—	—
22	Skin tuberculosis	—	—
23	Secondary syphilis	+	+
24	Primary syphilis	+	—
25	Chancroid	—	—
26	Chancroid?	—	—
27	Condyloma accuminata	—	—
28	Primary syphilis	+	+
29	Chancroid	—	—
30	Secondary syphilis	+	+
31	Chancroid	—	—
32	Chancroid	—	—
33	Chancroid	—	—
34	Chancroid?	—	—
35	Secondary syphilis	+	+
36	Chancroid?	—	—
37	Chancroid?	—	—
38	Secondary syphilis	+	+
39	Chancroid?	—	—
40	Primary syphilis	+	+
41	Secondary syphilis	+	—
42	Primary syphilis	+	+
43	Secondary syphilis	+	+
44	Chancroid?	—	—
45	Secondary syphilis, late	—	—
46	Chancroid	—	—
47	Chancroid?	—	—
48	Chancroid?	—	—
49	Chancroid?	—	—
50	Chancroid?	—	—

In two cases of Vincent's gingivitis carbolfuchsin stained the spirochetes well, but Parker 51 ink did not. A culture strain of Leptospira canicola did not take up the stain. Attempts at staining spirochetes in fetal lung tissue have failed thus far. Additional bacteriologic studies on the mechanism of this stain are under way in the dermatology service.

The methods described in the past have all had the disadvantage of being rather complicated and time-consuming in preparation.[3] Salles Gomes [4] reported a simple technique of staining Treponema pertenue and other spirochetes with Parker 51 superchrome blue-black ink. This ink contains, according to the manufacturer, a special patented dye called diaminostilbene disulfonic acid coupled to two moles of 1-amino-8-naphthol-2,4 disulfonic (Chicago) acid. It also contains 0.67% sodium hydroxide. Unfortunately, no other details were available from the manufacturer.

The method is as follows:

1. Place a drop of serum and a small drop of Parker 51 blue-black ink on one end of a clean glass slide.
2. Smear out rapidly as in making a blood smear.
3. Allow to dry. This takes about two minutes.
4. Examine under high dry or oil immersion lens.

The spirochetes stain blue-black against a light blue granular background. Specimens have now been kept without any change in color for more than twelve months.

We have used this staining method concurrently with dark-field examination in 50 cases of infectious syphilis and have obtained good correlation. Results are presented in the accompanying Table.

3. Levine, B. S.: Staining Treponema Pallidum and Other Treponemata, Pub. Health Rep. **67**:253-257 (March) 1952. De Lamater.[2]

4. An Easy and Rapid Method for Staining Treponemas, Foreign Letters, J. A. M. A. **148**:135 (Jan. 12) 1952.

ELECTRODESICCATION

A NEW METHOD OF APPLICATION

MILTON S. HARTMAN, M.D.
BROOKLYN

It is very often necessary to resort to destructive measures in long-standing, localized, pruritic, lichenified, and hypertrophic dermatoses that have not responded to conventional therapy, including x-ray treatment.

For this purpose the most commonly used agents are phenol, trichloroacetic acid, solid carbon dioxide, and electrodesiccation.

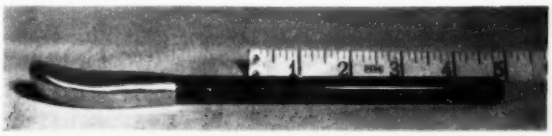
It is my aim in submitting this paper not to compare methods or to recommend the best one, but simply to introduce a new way of applying the electrodesiccation current.

When desiccating tissue, the operator finds it difficult to cover much ground using the ordinary needle electrode. It has therefore occurred to me to use the ordinary straight-handled, metal, prostatic electrode. This is admirably suited for the purpose because of its blunt tip, anterior concavity, and posterior convexity. By manipulation the operator can obtain the desired concentration or diffusion of spark and will find the curvatures readily adaptable to all surfaces. Moreover, effects far short of destruction, such as erythema, with or without exfoliation, can be easily obtained.

The effect produced is governed not only by the amount of current employed, but also by the area of electrode applied to the tissues and the speed with which it is moved over the surface. A small current can produce more destruction than a larger one if the electrode is allowed to rest on the surface; whereas, if the electrode is kept in motion, a larger current may result in nothing more than erythema and exfoliation, or perhaps no reaction at all if the speed of movement has been sufficiently rapid.

Sometimes simply moving the electrode back and forth with rapidity over the involved area, thereby effecting simple counterirritation, will be found of value in lessening pruritus. For this the prostatic electrode is particularly useful because of the ready adaptability of its contours to those of the surfaces treated. This method of application is especially useful in pruritus of psychogenic origin, in which therapy by suggestion plays such a major role. Large areas can be treated with ease. Of course, here only erythema, with or without exfoliation, and no stronger effect, is desired.

It is my clinical impression that alopecia areata is more responsive to this procedure than to the conventional phenol-ultraviolet combination. An exfoliative application is given. The advantage here is that large areas can be treated at one sitting. One hesitates to use phenol on larger than palm-sized areas because of the danger of absorption. However, therapeutic claims in this condition are always controversial.



Straight-handled, metal, prostatic electrode.

Anal, scrotal, and vulvar pruritus may be benefited by repeated mild applications. It is more often necessary to use more intensive doses, even destructive ones, in order to relieve the patient of this affliction.

Sluggish leg ulcers may be helped and even cured by repeated mild applications through a thin layer of gauze. The effluve has an irritative effect, thereby stimulating the growth of granulation tissue. It is also productive of ultraviolet radiation and ionizes air, thereby bathing the area in ozone. It is therefore bactericidal. Moreover, it produces mild anesthesia, which is, of course, fleeting. These by-effects must also be considered in the evaluation of this modality, not only in treating leg ulcers but in management of every condition for which it is used in doses short of destruction.

If the surface is exceedingly thickened, lichenified, and hypertrophic, it may be necessary to use local anesthesia in order to obtain adequate destruction.

The prostatic electrode is easily adaptable to any high-frequency spark-gap unit and may be obtained at any surgical dealer or manufacturer of high-frequency apparatus.

711 Bushwick Ave.

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

William Leifer, M.D., President

Henry Silver, M.D., Secretary

Feb. 21, 1952

Ehlers-Danlos Syndrome. Presented by Dr. Frances Pascher and (by invitation) Dr. Abram Kanof.

P. G., a white boy aged 5 years, was admitted to the pediatric ward of the Jewish Sanitarium and Hospital for Chronic Diseases, of Brooklyn, because of weakness and hypermobility of the joints since birth.

There is no parental consanguinity. The father and a cousin are known to be "double-jointed."

Examination reveals dermatorrhexis, dermatochalasis, and arthrochalasis. The skin of any part of the body can be stretched 8 to 10 cm., snapping back promptly when released. The integument has a soft pleasant feel, bruises readily, with the development of ecchymoses, and shows a few papyrus-like scars over the knees. The tourniquet test is strongly positive, and ecchymosis after drawing blood for analysis is tremendous. The general looseness and hypermobility of all the joints is striking, occurring to the extent that the hips are both dislocated and the child cannot walk. The fingers can be stretched to almost twice their length, and many joints can be rotated at will in any direction.

The roentgenograms revealed retarded epiphyseal development and osteoporosis of the spine, metacarpals, and bones of the forearm. Chemical analysis of the blood showed normal values throughout. The glucose tolerance curve on two different occasions was normal. The cellular content of the blood showed no significant change except for an eosinophile count of 78 per ml. (normal 109 to 359 per ml.). Chemical analysis of the urine showed normal quantities of oxyketosteroids; high normal to somewhat increased amounts of 17-ketosteroids in three different 24-hour specimens (3.94 mg., 2.5 mg., and 2.9 mg., normal 6 to 2.0 mg.), and an altered uric acid-creatinine ratio of 1.8 (normal less than 1.0).

In the Jewish Hospital and Sanitarium for Chronic Diseases, under the supervision of Dr. Samuel Feuer, a course of activity, passive and active, to tighten the fibrous structures about the hip joints was undertaken and successfully carried out. The boy now walks.

Ehlers-Danlos Syndrome. Presented by Dr. Frances Pascher and (by invitation) Dr. Abram Kanof.

L. B., a white girl aged 5 years, was admitted recently to the Jewish Sanitarium and Hospital for Chronic Diseases, of Brooklyn, because of difficulty in walking and mental retardation. The family history is negative.

Examination reveals hyperelasticity of the abdominal skin and a fine papyrus-like appearance of the skin of the hands. The finger joints and wrist joints are hyperextensible. Ecchymoses appear on the extremities from time to time. The clitoris is enlarged.

Roentgenographic examination revealed subluxation of the left hip joint and abnormal epiphyseal development of the upper extremities.

A 24-hour specimen of urine contained 3.5 mg. of 17-ketosteroids (normal under 2.0 mg.).

DISCUSSION OF PRECEDING TWO CASES

Dr. Abram Kanof (by invitation): These two patients are presented for their clinical and theoretical interest. Clinically, they illustrate the complete form and the *forme fruste* of the disease. The boy illustrates how a rehabilitation program can ameliorate the disability arising from the loose joints.

Theoretically, we were interested in the clinical and laboratory resemblances between Ehlers-Danlos syndrome and Cushing's syndrome or some other forms of adrenal hypercorticism: dermatorrhexis, delayed healing, fragile blood vessels, acrocyanosis, delayed epiphyseal development, osteoporosis, increased excretion of 17-ketosteroids in the urine, increase in the uric acid-creatinine ratio in the urine, and eosinopenia. Moreover, recent histological studies, particularly those using the electron microscope, have shown that the pathology in Ehlers-Danlos syndrome is not an overabundance of the elastic tissue but a fragmentation and diminution in the collagen.

Increased adrenal function may be of four types. Increased secretion of N hormone in the older child is secondary to a cortical tumor and gives rise to the adrenogenital syndrome. Not infrequently cases occur in which there is increased secretion of N hormone from birth or before birth due to diffuse hypertrophy of the cortex; this is the congenital type and gives rise to early adrenogenital changes. When increased amounts of S hormone occur in an older child, this is secondary to a tumor of the adrenal cortex and gives rise to Cushing's syndrome. There has never been described as such a case of diffuse congenital hypertrophy of the adrenal with excess formation of S hormone. We suggest that cases of Ehlers-Danlos syndrome may fall into this category. I need not emphasize that the delineation between S-hormone symptoms and N-hormone symptoms is not absolute in any patient with adrenal disease. Our boy would fit more neatly into this scheme if his oxysteroids instead of his 17-ketosteroids were elevated. The little girl shows an increase in her oxysteroid excretion, but she also has increased excretion of her 17-ketosteroids and manifests some evidence of virilism. Such lack of conformity is, however, the rule rather than the exception.

DR. DAVID BLOOM: The fact that Ehlers-Danlos syndrome is due to a disturbed embryonal development of the mesenchyme based on germ-plasm mutation partly elucidates the etiology of this abnormality. However, the fact that this is a hereditary disease should not discourage further investigation in regard to the pathogenesis. On the contrary, such studies are highly desirable. There are a number of examples of hereditary diseases in which such investigations contributed considerably to the clarification of the disease and led to the discovery of useful information. The study of Dr. Kanof is therefore commendable.

However, even if it could be proved that the Ehlers-Danlos syndrome is definitely associated with hypercorticalism, it would still have to be proved that the cutaneous syndrome is subordinate to the endocrinologic disturbance. But the findings of Dr. Kanof are not sufficient to consider a definite association with hypercorticism in his cases. Nevertheless, his study will be a stimulus to investigation in this direction of other cases of Ehlers-Danlos syndrome.

DR. LAURENCE L. PALITZ: Dr. Kanof has given us an interesting concept in relating this syndrome to hypercorticalism. Although not the first to suggest an endocrinopathy, he is, I believe, the first to point to the adrenal gland as a factor. The symptoms as presented would tend to incriminate the adrenal, but we find that, taken individually, many of them can be seen in other endocrinopathies and in nonrelated diseases. For example, fragility of vessels and dermatorrhexis can be seen in pituitary disturbances, avitaminoses, purpuras, and other diseases. Weakness is also a prominent symptom of hypoadrenalism, and osteoporosis is seen in abnormal parathyroid-pituitary conditions as well as in eunuchoidism, sarcoidosis, and other diseases. I think an important question is what happens to the skin in known cases of hypercorticism. Do we ever see skin changes in these cases comparable to those seen in the Ehlers-Danlos syndrome? The answer, I believe, would have to be "no." On the contrary, the skin in Cushing's disease becomes hard and coarse, and I have seen no reports in the literature concerning the appearance of changes similar to cutis laxa in individuals given corticotropin over long periods of time. Mussio Fournier, in an interesting treatise on skin changes in the endocrinopathies (Mussio Fournier, J. C.; Piaggio Blanco, R. A., and Cerviño, J. M.: Piel y anexos y glándulas endocrinas, Buenos Aires, Salvat Editors, S. A., 1944), cites several cases of cutis laxa in persons with known hypofunction of the pituitary gland and on this basis suggests a relationship between Ehlers-Danlos syndrome and hypofunction of the pituitary. Dr. Kanof has certainly given us more evidence relating this syndrome to some endocrine disturbance, but the question as to whether the gland involved is the pituitary, the adrenals, or both will have to await further evidence.

DR. MABEL G. SILVERBERG: There was remarkable improvement in the boy as a result of reeducation and physical therapy, and this is the most hopeful aspect of Dr. Kanof's presentation.

DR. VICTOR H. WITTEN: Dr. Kanof is to be congratulated for considering the possible relationship between the endocrinologic findings and Ehlers-Danlos syndrome, for correlating these findings with this syndrome, and for the clarity of his presentation. Of course, as Dr. Palitz has remarked, studies of this type will necessarily have to be carried further if definite cause and effect relationships are to be established. It was Dr. Pascher who recalled Ronchese's reports of epidermolysis bullosa-like lesions in some cases of Ehlers-Danlos syndrome and suggested that definite cases of epidermolysis bullosa be studied for evidence of hypercorticism. We therefore examined a boy, aged 3 years, with typical epidermolysis bullosa, at the New York Skin and Cancer Hospital. Our studies were modeled after those done by Dr. Kanof on his patients. The only finding that possibly might have been considered abnormal was a low eosinophile count. Dr. Sulzberger and I studied another case in private practice, that of a boy aged 9 years, who presented an eruption suggestive but not typical of epidermolysis bullosa. The one abnormal finding in this case was the presence of uroporphyrins. In neither of the cases we have investigated is the diagnosis of hypercorticism justified.

DR. CHARLES WOLF: Since Dr. Kanof made the adrenal gland suspect in Ehlers-Danlos syndrome and since these children with this condition do not live to a ripe age, I wonder if he knows of any reports on autopsy findings which suggest congenital adrenal disease.

DR. FREDERICK REISS: At the Montefiore Hospital we had under observation a patient with Ehlers-Danlos syndrome and advanced tuberculosis who had to undergo surgery. I suggested large doses of ascorbic acid for wound healing. The wound healed normally after the operation.

DR. DAVID BLOOM: Both children are conspicuous because of the large size of their heads. Is this due to hydrocephalus? As far as I remember I have not seen or read about this abnormality being associated with Ehlers-Danlos syndrome.

DR. FRANCES PASCHER: I should like to comment on the report of an eosinopenia in these cases. The number of eosinophiles was found to be reduced on one determination. One cannot draw any conclusions from a single count. It has been well established that there is a marked diurnal variation and a significant minute to minute fluctuation in the eosinophile count. A physiologic dip of 20% midmorning (this drop may be as great as 50%) and a 30% rise at midnight can be demonstrated in most individuals. One would have to do repeated counts at stated intervals on successive days before hazarding a diagnosis of eosinopenia or eosinophilia.

I should also like to ask Dr. Kanof whether or not a therapeutic approach can be formulated on the basis of the endocrinologic findings.

DR. ABRAM KANOF (by invitation): There are several points I should like to emphasize in the discussion. First, the suggestion that "it cannot be endocrine because the germ plasma is abnormal" is not an entirely correct point of view. As Dr. Bloom pointed out, diabetes is a hereditary disease. Dr. Priscilla White treats pregnant diabetic women with pituitary hormones. Babies of diabetic mothers are often born prematurely or die soon after birth, for there is proved hormonal disturbance in these mothers and babies which causes the babies to die quickly. They cannot be saved by insulin but have to be treated by gland medication ante partum. There is a disease definitely genetic in origin; nevertheless, the mechanism is endocrinal and the approach to treatment is endocrinal. The fact that the disease is genetic does not, it seems to me, rule out a glandular dyscrasia as a possible explanation for the genetic disturbance.

I am also interested in Dr. Palitz' discussion. He is disturbed by the fact that one sometimes sees hypopituitarism and hyperpituitarism in the same patient. That this may occur is fairly well recognized. Many of Cushing's original cases showed mixtures of hypoadrenalism and hyperadrenalism. In children with Cushing's syndrome the disease is due to overproduction of the S hormone; nevertheless, most of these children die of Addison's disease.

The question was also raised as to why some of the symptoms of Ehlers-Danlos syndrome do not appear in patients who receive large doses of corticotropin. It is also noted that the sequelae attributable to corticotropin therapy subside when therapy is withdrawn. The difference

may be that the child with Ehlers-Danlos syndrome has been subjected to corticotropin in utero; this may account for the changes being permanent, as well as for the types of changes.

Most babies with Ehlers-Danlos syndrome reported in the literature are eight-month premature. This is of interest because children of diabetic mothers also tend to be premature.

I am not prepared to say much about autopsy findings since I have not seen any reports on the subject. There have been many reports of histologic findings, however. Children with Ehlers-Danlos syndrome do not necessarily die young; they live highly protected lives.

The large head in the case of the boy and other patients with this syndrome is apparently not hydrocephalic since the measurements are within normal limits.

Dr. Pascher's question about endocrinologic therapy is interesting, since we have been considering it. In a case of hypercorticism with adrenogenital changes, Talbot has done a very interesting thing. He has administered cortisone to these children. The theory is that the extraneous cortisone depresses the child's production of cortical hormone. Talbot has reported eight patients thus far who have been quite successfully treated. I have observed one infant aged 6 to 7 months, with congenital adrenal hypertrophy and virilism. I gave her large doses of cortisone, after which the urinary ketosteroids dropped below their level at the time of admission. In other words, the administration of cortisone diminished the patient's output of ketosteroids. I am planning to treat our patients with large doses of cortisone and to study the effect.

Lepromatous Type of Leprosy (Hansen's Diseases). Presented by DR. JULIUS H. POLLOCK.

J. M., a man aged 20, a mechanic by occupation, was born on the island of Malta. He came to this country in 1946 and has remained here. He states that since 1946 he has been free of skin trouble until ten months ago, when an eruption developed in the lower extremities accompanied by frequent attacks of epistaxis.

When he was first seen, eight weeks ago, examination revealed an eruption involving the ear lobes, ankles, legs, thighs, and arms. The unit lesion was a nodule ranging in size from a pinhead to a pea, single and conglomerate, and of various hues from pink to deep red and violaceous. There was sensory loss to tactile discrimination on the dorsum of the left forearm. There was slight alopecia of the outer third of the eyebrows.

Nasal smears and skin scrapings were positive for acid-fast bacilli. Urinalysis and serologic tests for syphilis were negative. The complete blood cell count was normal, with the exception of a white cell count of 13,300.

Histologic examination of a nodule taken from the leg revealed solid sheets of reticulum cells packed with acid-fast bacilli of typical configuration. No tubercles were seen. The microscopic diagnosis was nodular type of leprosy (Hansen's disease).

The patient was placed on "sulphetrone." On the 10th day after the start of this medication the patient experienced a leprotic reaction. The drug was continued with eventual defervescence of the reaction. At the end of a course of "sulphetrone" the patient was placed under dihydrostreptomycin therapy. It is our impression that there has been a much greater response to the latter therapy than to the sulfone.

The family history is of epidemiologic interest. The mother, who emigrated with the above patient, is free of any signs of leprosy. The father, who has been here, is said to be free of the disease. However, the brother who came with the patient at the same time is under our care with what appears to be the indeterminate type of leprosy. His lesions are mainly of the macular type. He has marked peroneal involvement on both sides and positive skin and mucous membrane scrapings. He has refused to allow a biopsy. This patient was also placed under "sulphetrone" and dihydrostreptomycin therapy, but he has not shown nearly as great a response as the presented patient has shown.

DISCUSSION

DR. JULIUS H. POLLOCK: While under treatment with sulfones this patient developed a leprotic reaction. The medication was continued, and the reaction subsided. During his rest period from the sulfones, the patient was placed on dihydrostreptomycin, and there seems to be a more marked flattening of the lesions under this therapy than occurred with sulfone therapy.

The lepromin skin test, when positive, is of special value in the tuberculoid type of lepra, in which bacteriological demonstration is sometimes difficult; it is of still greater value as a prognostic test, and also as an indication of therapeutic progress. Inasmuch as the test, which is negative in the nodular type of leprosy, will become positive over a period of time if there is clinical involvement, and as, conversely, in those patients in whom therapy is ineffectual or in cases of persistence of the negative reaction, it points to a bad prognosis as with the tuberculin test, the reaction is not static and varies with the allergic relationship between the patient and the leprosy bacillus.

DR. DAGUET, Paris, France (by invitation): Customarily we treat our patients during the period of untoward reaction to the sulfones with dihydrostreptomycin for one or two weeks, and generally this drug produces rapid results. However, it is necessary to follow the treatment with sulfones, at the same time increasing the dosage and frequently subjecting the patient to blood tests. It is important for the prognosis to follow the course of this disease. The lepromin test is probably negative for this patient at the present time. I have seen cases which showed proof of the efficacy of the sulfone treatment in producing a negative lepromin reaction.

DR. FREDERICK REISS: This case presents a number of interesting problems. First is the problem of segregation or isolation. I think isolation in this case is not necessary. I have searched about 60 to 70 years back in the literature, and I found only one patient who contracted leprosy in New York. Yet I believe that this patient should be segregated and that he should not come in contact with children. There is marked involvement of the ear lobes, which should be emphasized in relation to a diffuse lepromatous infiltration of the face. There is always a chance of finding bacilli in the ear lobes, even when the facial lesions have completely vanished. I believe there is no "pure type." I found definite sensory disturbance in this patient, which is apparent in an appreciable enlargement of the left ulnar nerve. The patients that I treated in this city also responded rapidly to sulfone therapy. The leprotic reaction is still rather puzzling. Is it a bacillemia, or are we dealing with a hypo or anergic phase of leprosy? Since the lepromin reaction is almost always negative, the leprotic reaction probably represents an anergic phase of leprosy. The preceding speaker is right, emphasizing that after dihydrostreptomycin has improved the leprotic reaction, treatment should be carried on with sulfone drugs. However, one has to watch carefully the red blood cell count.

DR. MORRIS LEIDER: Since the leprosy bacillus and the tubercle bacillus have close botanical kinship, any agent effective against the latter is worthy of trial against the former. Just this morning, newspaper publicity has appeared concerning a new group of antituberculous agents, namely isonicotinic acid hydrazides. If they are to any extent as effective against leprosy as they are believed to be against tuberculosis, agents with possibilities equal to those of penicillin against syphilis are at hand.

DR. ABRAHAM J. ORFUSS: Just after World War II, some of us considered the possibility of leprosy being brought back by returning members of the armed forces who served in endemic areas. At the Veterans Administration Clinic, with which I am associated, we are treating five ex-soldiers with leprosy. In none was it possible to prove that the disease was contracted during military service, since all came prior to military service from endemic areas.

DR. F. SERRI, Pavia, Italy (by invitation): I recently returned from Habana, Cuba. While there I saw a number of the 400 patients at the leprosarium. All of the patients are doing well on sulfones; dihydrostreptomycin is used only when there is an untoward reaction to the sulfones.

DR. JULIUS H. POLLOCK: I wish to point out that Dr. Saenz (Saenz, B.: Lepra Reaction: Its Treatment with Dihydrostreptomycin, A. M. A. ARCH. DERMAT. & SYPH. **65**:59-69, 1952) not only used dihydrostreptomycin for the leprotic reaction but also during the rest periods from the sulfones.

As to segregation in this city, being a Department of Health official, I can tell you that the attitude is not to "isolate" the leper. We certainly do not restrict the patient with lepra of the tuberculoid type with minimal skin changes, even though there may be positive nasal or skin scrapings, which are not common in this type. The patient with the nodular type of lepra, if he has open lesions, is restricted in the sense that he is taught to use his own culinary utensils and bedding and not to engage in food-handling. The family is also instructed about the need for avoiding contact, especially in the case of young children or infants, since they are especially vulnerable.

A diagnosis of leprosy is never made by us for a patient in the absence of knowledge of contacts or a geographical history, unless, along with the positive nasal and skin scrapings, histological study demonstrates the typical architecture of the disease and, if possible, the presence of the bacillus in the tissue. Neglect of such caution can cause much damage to the patient.

Lupus Vulgaris. Presented by DR. DAVID BLOOM and (by invitation) DR. FERNANDO SERRI.

C. C., a Chinese man aged 21, who came to the United States three months ago from Hong Kong, has had an eruption on the right cheek for the past six months. It consists of two quarter-sized round lesions, each of which is made up of tiny erythematous nodules. The lower lesion is reddish brown, the upper one is red.

Laboratory examinations consisting of serologic test for syphilis, complete blood cell count, erythrocyte sedimentation rate, and urinalysis gave normal findings, except for leucopenia (4,000 leucocytes). The intradermal tuberculin test gave a 1 + reaction in dilution of 1 : 1,000,000 and a 2 + reaction in dilution of 1 : 100,000. Scrapings from the lesions and from the nasal mucosa did not reveal any acid-fast bacilli. A lepromin test was strongly positive after 48 hours, but a histamine test gave a normal reaction. Roentgenogram of the chest did not reveal any abnormal finding. The histologic report was sarcoid reaction.

DR. JULIUS H. POLLOCK: When I first saw the patient at the New York Skin and Cancer Hospital, my impression was that it was an instance of sarcoid. Tonight, although the lower pole of the patch is somewhat erythematous, the absence of the play of colors and the papular or papulonodular formation with the scaling and the so-called apple-jelly nodules, suggest to me sarcoid. Again Jessner's use of the term "transient form" makes me wish to repeat what I said some time ago, when I presented a patient with lupus miliaris disseminatus faciei, that we err if we bind our morphologic conceptions of cutaneous tuberculosis to static forms. The determining factor for the morphology is the allergic or absence of allergic reaction between the bacillus and the host. This reaction is labile and hence accounts for the "transient forms" that may show the absence of one feature or the presence of another in the same individual with cutaneous tuberculosis.

DR. F. SERRI, Pavia, Italy (by invitation): In view of the marked hypersensitivity of the patient to tuberculin, the diagnosis of sarcoid is not likely. The clinical appearance, too, is against sarcoid but suggests lupus vulgaris. Jessner's view that sarcoid reaction occurs in lupus vulgaris is generally accepted.

Lupus Erythematosus in a Chinese. Presented by DR. ABRAHAM J. ORFUSS.

R. C., a Chinese man aged 57, registered at the department of dermatology of the New York University-Bellevue Medical Center on Jan. 8, 1952, presenting several erythematous lesions on the face, characterized by an edematous border and adherent scaling.

The lesions are scattered over the left eyebrow, preauricular regions, left nasolabial fold, and lower lip. There are several similar lesions on the upper back. There is scarring on the right cheek and "V" of the neck.

Routine serology for syphilis was negative. The sedimentation rate was 2 mm. per hour (normal 10 mm. per hour). The complete blood cell count showed 4,500,000 erythrocytes, 100% hemoglobin, and 7,200 leucocytes with 74% neutrophiles, 23% lymphocytes, 1% eosinophiles, and 2% monocytes.

Histologic examination revealed a dense cellular infiltration of a banal type in the cutis. The infiltration was particularly dense in the periadnexal area. There was some basophilic degeneration throughout the cutis, and marked edema was present throughout. Dilated vessels were present. Some liquefaction of the basal cell layer was seen. The overlying epidermis had no features of pathological significance except for the basal cell liquefaction noted and hyperkeratotic plugging. Weigert's stain for elastic tissue was normal.

DISCUSSION

DR. FREDERICK REISS: Lupus erythematosus is just as rare as pernicious anemia or sprue in the Chinese. It is almost nonexistent in China. During 19 years in China I saw only a few cases of lupus erythematosus of the discoid type.

DR. ABRAHAM J. ORFUSS: Review of the literature failed to reveal that lupus erythematosus is found frequently in the Chinese. It is described as not being as common in the tropics as in the temperate zone, although its occurrence in the tropics is by no means exceptional. I found one reference to lupus erythematosus in a Chinese (Yang, K. L.: Lupus Erythematosus with Unusual Changes in Finger Tips and Nails, *Acta dermat.-venereol.* **16**:365, 1935), but this reference makes no mention of its frequency among the Chinese.

Adenocarcinoma of the Large Bowel (Metastatic?). Recurrent Lupus Vulgaris After Cessation of Calciferol Therapy. Presented by DR. JOHN GARB and DR. CHARLES F. SIMS.

A Case for Diagnosis: Granuloma Annulare? Necrobiosis Lipoidica? Presented by DR. MORRIS LEIDER.

Extensive Epithelioma of the Scalp Combined with Gumma. Presented by DR. DAVID B. BALLIN.

A Case for Diagnosis: Hypertrophic Lichen Planus? Prurigo Nodularis? Presented by DR. IRWIN I. LUBOWE.

A Case for Diagnosis: Macrodactylia with Clubbing of the Left Index Finger? Periungual Fibromatosis? Recklinghausen's Disease (Forme Fruste)? Presented by DR. FRANCES PASCHER.

Perifolliculitis Capitis Abscedens et suffodiens. Presented by DR. WILLIAM M. SISKIND.

Dystrophia Unguium Mediana Canaliformis. Presented by DR. FREDERICK REISS.

Dystrophia Unguium Mediana Canaliformis. Presented by DR. DAVID BLOOM and (by invitation) DR. FERNANDO SERRI.

Recklinghausen's Disease. Presented by DR. RAPHAEL BREAKSTONE.

NEW YORK DERMATOLOGICAL SOCIETY

Anthony C. Cipollaro, M.D., *President*

Maurice J. Costello, M.D., *Secretary*

March 25, 1952

A Case for Diagnosis: Papulonecrotic Tuberculid? Erythema Nodosum Perstans?

Presented by DR. MAURICE J. COSTELLO.

DISCUSSION

DR. FRANK C. COMBES: This type of eruption has been described as occurring only in young girls. I have never seen it in a male. It is always associated with a poor peripheral circulation and an edematous extremity. I have never seen it in thin, shapely legs. Many of its features do resemble papulonecrotic tuberculid, but I have never been convinced that all instances are manifestations of a real toxic tuberculid as described by Darier. These lesions may be associated with streptococcal infection, gastrointestinal disturbances, dermatitis medicamentosa (iodides and bromides), acute rheumatic fever, and other systemic intoxications. I have seen several cases respond after the administration of cod liver oil. I do not think the relationship to tuberculosis exists in all cases.

DR. WILBERT SACHS: I agree with the diagnosis of papulonecrotic tuberculid, but because of the vascular changes I would like to call it a possible dermatitis necrotisans, which I believe is a form of papulonecrotic tuberculid.

DR. EUGENE F. TRAUB: Isn't this the picture Dr. Combes described as chilblain circulation, occurring fairly exclusively in young women? I don't know what the nodules represent, unless it is some type of tuberculosis.

DR. PAUL E. BECHET, Elizabeth, N. J.: I would be inclined to think it was papulonecrotic tuberculid, perhaps in an atypical form. The lesions are discrete, papular, nodular, and inflammatory. Varioliform scarring exists in some areas.

Moniliasis Avitaminosis.

Presented by DR. GEORGE C. ANDREWS.

R. V., an Italian girl aged 14, was previously presented before the New York Dermatological Society on Oct. 26, 1943. She has had an eruption of the face, scalp, mouth, trunk, and extremities since the age of 4. She first consulted me in 1943, because of a sore mouth. Cultures at that time, checked by Dr. Rhoda Benham, showed Candida albicans. Since then the child has been under my care, and all remedies that might possibly be beneficial have been tried, including ethyl iodide inhalations (hydriodic ether), folic acid, iodides by mouth, crude liver extract injections, vitamin B_{12} injections, calciferol, and thyroid extract. Locally, she has used Castellani's paint, iodine petrogen® 5%, iodine tincture, and other topical remedies.

The cutaneous lesions are unique. Their symmetry and configuration resemble psoriasis clinically, especially on the chest. There is marked alopecia and atrophy on the scalp, which at times has been diagnosed by other physicians as favus.

She is being presented again today for further suggestions as to treatment, with the hope that Dr. Lewis may have some antibiotic against fungi which could be tried in her case.

DISCUSSION

DR. GEORGE M. LEWIS: It is an unusual and most interesting case. The diagnosis of moniliasis is confirmed, although I would also entertain the possibility that there is a mixed fungous infection and that many of the lesions now present are due to Trichophyton (purpureum) rubrum. One might consider a T. rubrum infection of the nails and palms, and the generalized eruption would fit in with that as well. It is possible also that Candida albicans is mimicking that organism, but I suspect the other fungus may be present in deeper strata and might be found on repeated examinations. The tongue is typical for moniliasis.

DR. J. LOWRY MILLER: I recall that when we were working on undecylenic acid, Dr. Andrews lent us this patient, and we had similar results. We were able to culture C. albicans from the lesions on the body, scalp, mouth, and nails at that time. I think we did repeated cultures at that time and never found any other organism.

DR. GEORGE M. LEWIS: Has she ever had chronic paronychia? She has none at this time, which is unusual if C. albicans is widespread.

DR. WILBERT SACHS: I should like to ask Dr. Lewis what results have been obtained by changing the intestinal flora in these patients with moniliasis.

DR. EUGENE F. TRAUB: The patient presents much telangiectasis on the scalp. Is that because of x-ray treatments she has received, or is it part of the cutaneous changes that might go with the disease?

DR. GEORGE M. LEWIS: I wonder if the family could be examined for a possible focus of T. rubrum infection. I assume this child is vulnerable to fungous diseases.

DR. GEORGE C. ANDREWS: I have examined the father, mother, sister, and aunt. Whether there are more members of the family I don't know, but none of those have signs of disease of the nails, or favus, or any fungous infection that I know of. I didn't examine the feet. As Dr. Miller has said, Dr. Hopkins and Dr. Benham studied this patient for about two years, made various cultures, and were in full agreement that it was a case of moniliasis. We never got any other organism. The stools, mouth, skin, and nails were loaded with C. albicans. The lesions have changed throughout the years. Originally the body was not much involved. Now the body is more affected, and there is less on the face. At one time the patient was given ethyl iodide inhalations and potassium iodide by mouth, and a tuberous iodide eruption on the scalp developed like horns. I thought at the time that it was an unusual fungous infection of the scalp and showed the patient at the Manhattan Dermatologic Society, but I later found that it was an iodide eruption. It has been difficult to arrange for this patient to go to school. I don't recall that she ever had x-ray treatment to the scalp, although she may have had it before she came to us. She was on a high-protein diet for a year or more and received acidophilus milk and beta lactose without much change in her condition.

Leucoplakia. Presented by DR. FRANK E. CORMIA.

A. K., a generally healthy white woman aged 43, was presented before this society on Jan. 22, 1952, with leucoplakia of some eight months' duration. At that time the opinions of the members were divided, some favoring destructive measures and the others advocating symptomatic therapy, including vitamins and crude liver extract. During the two months' interim, the patient has been treated with injections of crude liver extract and, in addition, has taken vitamin B complex in large doses and 50,000 units of vitamin A daily. The use of hot and spicy foods and tobacco has been stopped.

There has been improvement in some areas and slight progression in others. There is evidence of extension posteriorly, while partial involution has occurred anteriorly on the tongue.

DISCUSSION

DR. GEORGE C. ANDREWS: I feel as Dr. Costello does that it is important to rule out lichen planus, because of the annular appearance along the posterior edge and because of the homogenous and smooth central portion which is not broken down or torn. All that thin area is an entirely smooth surface, not at all ulcerated. In leucoplakia we would expect some breaking down with a lesion of that extent. It is important to do several biopsies. I have in mind a similar case, in which the fifth biopsy specimen showed carcinoma of the tongue, and a hemiglossectomy was necessary. One has to be very cautious in handling this case.

DR. LESLIE P. BARKER: Today I am more inclined to make a diagnosis of lichen planus than of leucoplakia, although treatment by electrodesiccation may have changed the clinical picture. Another biopsy specimen should be taken in an endeavor to establish a positive diagnosis.

DR. WILBERT SACHS: I have had the opposite experience from that of Dr. Andrews—a case diagnosed as epithelioma, which from the slide was ordinary lichen planus. In this case I would certainly think of lichen planus. However, when the patient was shown two months ago, the question was not whether the disease was lichen planus but whether it was epithelioma on leucoplakia. I don't know if the lichen planus is a new condition, but I don't see how it could have been present then. Microscopically, two months ago, the condition was leucoplakia. We did think of lichen planus, but I could not make that diagnosis at that time.

DR. EUGENE F. TRAUB: I discussed this case with Dr. Sachs and asked him whether he could look at a section of an oral lesion like this one and see a picture that might fit into the diagnosis of leucoplakia, and have at the same time a section taken from another part of the lesion which looks like lichen planus. He admitted this could happen. With the change that has occurred in this lesion since we saw the patient before, I would now make a diagnosis of lichen planus. I saw a case of lichen planus on the same side of the tongue in a man about this same age. Radium had been used, and when I saw the patient the first time there was a peculiar ulceration and thickening I have never seen before in lichen planus. A section was removed which proved the presence of squamous cell epithelioma. The patient died following partial removal of his tongue. So lichen planus in the mouth can apparently be eroded and irritated enough to terminate as epithelioma.

DR. PAUL E. BECHET, Elizabeth, N. J.: It is difficult to believe that such extensive lesions limited entirely to the mouth could be lichen planus, without at least a few corroborating lesions elsewhere. In view of this, leucoplakia in my opinion is the better diagnosis.

DR. GEORGE M. LEWIS: The two patients with lichen planus of the mouth that eventuated into cancer had received radium treatment. I wonder whether unmolested lichen planus of the mouth is not rather a banal condition?

DR. LESLIE P. BARKER: If this is lichen planus, treatment should be instituted because persistent mucous membrane lesions of this disease may develop into epitheliomas. I have seen three such instances. One was in a man of 21 who had lichen planus only two years, in whom a squamous cell epithelioma developed on the lower lip. The other two cases were of men in their 50's who had had lichen planus on the skin many years previously and had had persistent mucous membrane lesions in which epitheliomas developed. Microscopic sections showed that these epitheliomas had developed on what was histologically lichen planus of the mucous membrane.

DR. WILBERT SACHS: Senile keratosis can sometimes mimic lichen planus. You might remove a lesion, thinking it was a keratosis or epithelioma, and it might turn out to be lichen planus.

DR. GEORGE C. ANDREWS: I have also had two patients with lichen planus of the tongue in whom epithelioma developed with fatal outcome. One of them, I am certain, had no radium treatment.

DR. FRANK C. COMBES: I would treat this patient with the utmost conservatism because with every biopsy you are going to traumatize the lesions, leave a new scar, and add to the chronic irritation. I certainly would not use radium. I think this patient has leucoplakia. I would increase the vitamin A dosage and cleanse the lesion daily with "ivory" soap on a toothbrush.

DR. J. LOWRY MILLER: I would go in between the suggestions made by the previous speakers. I would still treat this patient with liver. Part of the lesion has improved. If I took a biopsy specimen, it would be from that advancing border, which should be watched.

DR. ANTHONY C. CIPOLLARO: Regarding the incidence of carcinoma in lichen planus of the mouth, if one searched the literature one would not find as many cases as have been cited here this evening. From the literature, one would be likely to regard lichen planus of the mouth as of no great concern, disappearing of its own accord if not irritated. I do not advise active treatment of lichen planus of the mucous membrane. I have never seen cancer developing in lichen planus of the mouth.

DR. FRANK E. CORMIA: This lesion, as Dr. Andrews has pointed out, has spread. It started with a button-like plaque typical of leucoplakia. This was destroyed with electrocoagulation. It has since recurred peripherally and spread outward. I shall go on treating it conservatively for the time being, but if there is much more spread I shall perform another biopsy.

A Case for Diagnosis: Dermatofibrosarcoma Protuberans? Presented by DR. GEORGE M. LEWIS.

C. S. J., a woman aged 61, has had a painful tender nodule on the left arm for the past four years. A painful nodule first developed on the left arm 10 years ago. This was excised, and the pathologic report was that of Weber-Christian disease. A few years after the first nodule had been excised, another appeared in close proximity to the original site. This was treated by irradiation, dosage unknown, with disappearance of the lesion. In addition to the nodule which appeared four years ago, another lesion has since developed in a more proximal position on the arm.

There is a plum-colored, firm, subcutaneous tumor, 6 by 8 cm. in size, on the left arm. A second lesion, smaller but more deeply situated, is also noted.

Biopsy was interpreted as indicating chronic vasculitis with necrobiosis and fibrosis.

DISCUSSION

DR. WILBERT SACHS: I agree with Dr. Machacek that this is not dermatofibrosarcoma protuberans. There is a process that is deep, and I thought of some type of panniculitis. There is a definite area of necrosis. I also saw those large cells which would not speak against Weber-Christian disease. I should like to see more giant cells, which I did not see; however, with the depth of process and type of cells, I think it is some type of Weber-Christian disease.

DR. EUGENE F. TRAUB: There were two lesions, one was on the skin surface and had an inflammatory process supervening. It looked as if it were about to break down and was fluctuant and hot, with a few tiny superficial vesicles. Then, posteriorly, subcutaneous, and not attached, there was another large tumor that I couldn't identify unless it was a fibrous connective tissue or a fat tumor. I think it is very probably a form of panniculitis, as the first biopsy showed.

DR. PAUL E. BECHET, Elizabeth, N. J.: I have no diagnosis to offer, but if it was on my arm, I should like the whole tumor excised.

DR. FRANK E. CORMIA: It would be unusual to have Weber-Christian disease exist for such a long time without fever or any other evidence of the disease. Was there any evidence in the slide of syphilis?

DR. WILBERT SACHS: It is a deep process, with no evidence of syphilis.

DR. GEORGE M. LEWIS: The diagnosis of dermatofibrosarcoma protuberans was favored on clinical grounds because the lesions are very firm or fibrotic in character; they recurred after excision and progressively enlarged, with an uneven surface, as mentioned by Dr. Traub. The biopsy doesn't confirm the clinical impression. I am not sure it is Weber-Christian's disease. I shall try to get more sections.

NOTE: The lesions were later excised, and the histologic report was lymphosarcoma.

Chronic Lupus Erythematosus Treated. Presented by DR. FRANK E. CORMIA.

E. S., a woman aged 36, was previously presented before this society on Jan. 22, 1952. At that time there was an acute erythematous exacerbation of the eruption occurring with the menstrual period. Superimposed upon the acute lesions were evidences of secondary pyoderma.

Two days after presentation the condition became much worse, with infected crusted lesions on the face, scalp, and hands, and the patient was hospitalized. The temperature was 106 F.,

white blood cell count 3,300, and hemoglobin 10 gm. Culture of the cutaneous lesions yielded Pseudomonas aeruginosa, which was sensitive to streptomycin and chloramphenicol (chloromycetin®) and resistant to other antibiotics. Treatment with these two drugs was initiated in full dosage, and two transfusions were given. After five days the temperature approached normal, the erythematous and edematous lesions subsided, and the infectious element became minimal. Daily therapy with corticotropin (ACTH), 25 mg. by intravenous drip, was initiated, with injections of crude liver extract and use of chloramphenicol topically, for two weeks. By this time all signs of activity of the lesions had largely stopped. The corticotropin was tapered off and then discontinued, following which a complete hysterectomy was performed. Postoperatively the temperature rose to 104 F., and there was some return of the cutaneous lesions. Nine days after the operation corticotropin was resumed for another week, after which the patient was discharged from the hospital on moderate doses of cortisone and crude liver extract.

DISCUSSION

DR. LESLIE P. BARKER: Today I think there is little question of a clinical diagnosis of lupus erythematosus. There has been such spectacular improvement in the clinical picture that one can hardly recognize the patient as the same person. It is difficult to say whether castration or cortisone is responsible for this improvement.

DR. PAUL E. BECHET, Elizabeth, N. J.: I would agree with the diagnosis of chronic discoid lupus erythematosus, but one must always bear in mind the possibility that this can change into the disseminate type. In my opinion this is much more rare than is indicated by the statement in Ormsby and Montgomery's textbook "Diseases of the Skin" (seventh edition, Philadelphia, Lea & Febiger, 1948, p. 950), namely, that a third of the cases of subacute and acute disseminate lupus erythematosus develop from chronic discoid lupus erythematosus.

DR. GEORGE M. LEWIS: The clinical result at this time is so good that it is startling. We will hope that remission will be permanent.

DR. ANTHONY C. CIPOLLARO: This is the most beautiful result I have ever seen, considering that this woman was at death's door with a temperature of nearly 106 F., which probably had nothing to do with lupus erythematosus but was due to secondary infection. No doubt she improved a great deal with the combination of antibiotics and cortisone, but the question is, what has castration to do with it? If there had been no castration, would she have improved with use of corticotropin and the antibiotics? If castration improves acute disseminated lupus erythematosus, then it should be more widely used in moribund patients. A great deal more experience is necessary to evaluate this therapeutic procedure.

DR. EUGENE F. TRAUB: I don't believe Dr. Cormia attributes the improvement to castration, but I think he expects castration to prevent the recurrences and exacerbations that occurred at the patient's menses.

DR. FRANK E. CORMIA: I wrote Haserick and found that he has been using x-ray castration more or less routinely on older patients; he thinks it steadies them and makes their course less stormy. The gynecologists are much opposed to this procedure and feel that if castration is performed, it should be surgical.

Leprosy. Presented by DR. GERALD F. MACHACEK.

R. V., an exchange student from India aged 22, is presented from the Vanderbilt Clinic with lesions on the extensor surfaces of the arms and on the trunk of 10 months' duration. The lesions were not pruritic and did not respond to self-medication with penicillin ointment. They spread slowly, and at the time of the patient's first visit to the clinic, in June, 1951, they covered his entire body, being most numerous over the extensor surfaces of the arms and on the back and buttocks. There was no history of previous illness or eruptions and no history of contact with leprosy, although the patient comes from an endemic area.

Biopsy showed an atrophic epidermis which was slightly keratotic. There was a diffuse granulomatous infiltrate in the corium, separated from the epidermis by a narrow zone of connective tissue which was free from pathologic change. Infiltration was present in the perivascular areas, but there was no definite relation to nerves. Most of the cells were epithelioid, although a small scattering of mononuclear cells was present. The lesion was more proliferative

and less circumscribed than sarcoid. On histologic and clinical bases, the lesion was definitely one of leprosy. Acid-fast bacilli were present in sections stained by the Ziehl-Neelsen technique.

Neurologic examination showed areas of anesthesia and hypoesthesia over the center of the lesions, particularly those showing loss of pigment. There was no apparent thickening of the nerves, although the left ulnar nerve was palpable, and there was almost complete loss of sensation over most of its course.

The patient was given gradually increasing daily doses of sulfoxone sodium (diasone®) until a total amount of 0.9 gm. a day was reached. Except for some nausea and diarrhea during the first two weeks, he tolerated the medication well, and his lesions began to involute. At present there are few of the infiltrated type, and those are mainly over the left elbow. Because of the large number of acid-fast bacilli in the lesions he was also given dihydrostreptomycin, 2 gm. weekly.

DISCUSSION

DR. FRANK C. COMBES: This is the tuberculoid type, which is the commonest in New York. The patient shows atrophy of the thenar eminences, partially depigmented patches over the trunk, and enlargement of the ulnar nerves. These patients do quite well in this climate without therapy. They have a rather benign type of involvement which is not communicable.

DR. FRANK E. CORMIA: I wonder if the disease in this patient should be classified as the pure tuberculoid type, since Dr. Machacek found numerous bacilli. I think the patient has the indeterminate type of leprosy. He is at least potentially infective, and I think thorough treatment should be administered.

DR. FRANK C. COMBES: I meant that the tuberculoid type does well in this climate. I believe you can find the organisms in any of the cases.

DR. FRANK E. CORMIA: Patients with tuberculoid leprosy should be treated even when the disease shows spontaneous improvement, because the literature contains many examples of tuberculoid leprosy with temporary arrest, followed by later development of lepromatous features.

DR. GERALD F. MACHACEK: I am inclined to doubt that leprosy in this climate is as benign as is made out. You will recall the missionary, presented by Dr. Cannon for Dr. Sloane, with a solitary lesion on the back of the neck, which appeared 14 years after he left Burma. Satellite lesions and something of a lepra reaction developed after sulfoxone sodium treatment, with terrific neuritis and an exanthema. The patient went to Carville, La., and is now practically well. This man reacted very rapidly with a slight dermatitic type of reaction with only a few cells and quite different pathology, another argument which should militate against considering leprosy in this climate as benign. After wars such as the occupation of the Philippines, there are definite statistical indications that leprosy develops in those people who have spent some time in endemic areas somewhat more frequently than one would expect.

Hodgkin's Disease Complicated by Unusual Type of Erythema Multiforme Following Blood Transfusion. Presented by DR. MAURICE J. COSTELLO.

E. H., a man aged 53, is presented from Lenox Hill Hospital. He was first examined on July 28, 1949, because of enlargement of lymph nodes in the cervical region, thought to be caused by infectious mononucleosis. There was a rather high eosinophile count and anemia. Recently he was in the hospital for five weeks, being discharged on March 14, 1952. On that day he had a transfusion of blood. Three days later he felt ill, and his present eruption began to develop. On March 11, 1952, his hemoglobin was 73%, red blood corpuscles 3,400,000, and leucocytes 2,700, with 77 polymorphonuclear leucocytes (64 filamented, 13 nonfilamented), 30 lymphocytes, 2 monocytes, and 1 eosinophile. There was an occasional atypical lymphocyte, slight achromia and 2 Türk's cells. During his hospitalization a roentgenogram of the lungs showed bronchopneumonia and increase in the size of the hilar nodes. The heterophile agent was positive in a dilution of 1:28. The Davidson Trichinella test was negative. The bone marrow showed granular hyperplasia, especially of the eosinophiles, and there was erythroblast hyperplasia. The complement-fixation test was negative but recently had been positive. The erythrocyte sedimentation rate was 97 mm. per hour on March 17, 1952.

The patient is presented because of the bizarre eruption. The lesions are of three types: (1) the early lesions of odd shapes with a central crust surrounded by grayish-black coalescing

bullae, which in turn are surrounded by an area of pink erythema and small discrete vesicles in corymbiform arrangement; (2) guttate, tense, shotty bullae, surrounded by a thin halo of erythema, and (3) short-lived crusted lesions on the face, suggestive of generalized herpes simplex. The patient had several matchhead-sized vesicles on the hard palate.

The patient feels weak, but there is no elevation of temperature. He is receiving deep roentgen therapy at present. A biopsy has been performed, and virus studies are being carried out.

DISCUSSION

DR. GEORGE M. LEWIS: My diagnosis is herpes zoster with generalization. The unusual feature is the lack of zosteriform distribution. I prefer that diagnosis to varicella because of the patient's age and because the development of the lesions would be distinctly atypical for the latter disease.

DR. FRANK C. COMBES: I should prefer to call this a generalized zosteriform eruption. One feature against this is its multiform nature. The patient has bullae in all stages of development and involution, some with central necrosis and umbilication. I should be interested in the result of virus studies. In variola the eruption would be more uniform in nature.

DR. J. LOWRY MILLER: I favor a diagnosis of varicella for the reasons Dr. Combes mentioned. I don't recall any case of generalized zoster in which there was no tendency to localize along one area before generalization occurred.

DR. FRANK E. CORMIA: There are many puzzling features in this case. The man received penicillin, which could explain the erythematous and erythema multiforme type of lesions. It might be a dermatitis herpetiformis type of eruption associated with some abdominal cancer. I think virus studies should be made. Biopsies of the lesions could be performed and an attempt made to identify virus bodies in the lesions; chick embryo cultures could also be done. I don't think it is unusual to see necrosis in generalized herpes, particularly in debilitated patients. One other possibility would be a Hodgkin's type of infiltration superimposed on a herpetiform type of eruption, with resulting necrosis.

DR. LESLIE P. BARKER: This impresses me as being a virus infection, although I am not certain in which category to place it. I have never seen such a case of generalized herpes zoster without a typical zonal distribution of the primary lesion. The generalized lesions usually appear within a few days, accompanied by fever, and have a general appearance of the eruption of chicken-pox. They usually become umbilicated and are uniformly pea-sized. In this patient, however, the lesions vary in size from that of a large pinhead to 2 or 3 cm. in diameter; some are umbilicated, and some have an erythematous base. There is no zonal distribution of any of the lesions. This, with the multiplicity in size and types of lesions, would point against a diagnosis of generalized herpes zoster. It is not uncommon to see herpes zoster, even the generalized type, associated with lymphoblastomas.

DR. ANTHONY C. CIPOLLARO: This patient definitely has Hodgkin's disease, and we know that occasionally in that disease there are various types of cutaneous lesions. It would be a healthier attitude if we just considered these as manifestations of Hodgkin's disease, rather than to try to give the eruption a name. Internists would prefer that we do this, rather than try to give the disease a morphologic name, even though in the backs of our minds the morphologic name we give it be associated with Hodgkin's disease. So, for the record, I would say it is Hodgkin's disease associated with a vesicular or bullous eruption.

Scirrhous Carcinoma of the Breast. Presented by DR. ANTHONY C. CIPOLLARO.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Fred D. Weidman, M.D., *Chairman*

Bertram Shaffer, M.D., *Secretary*

Sept. 19, 1952

Kaposi's Sarcoma. Presented by DR. HENRY G. DECKER and DR. HERBERT LUSCOMBE.

W. W., a white man aged 72, presents over the face, neck, and trunk many purplish-red nodules and firm plaques varying in size up to about 5 cm. in diameter. The face has a leonine appearance. There is enlargement of the axillary, cervical, inguinal, and epitrochlear lymph nodes.

The patient noted the eruption in April, 1952. There was no itching or pain. In the last three weeks he has had a weak feeling in the stomach with shortness of breath.

Blood tests revealed 57.4% hemoglobin, 2,800,000 erythrocytes, 3,100 leucocytes, 24% polymorphonuclear leucocytes, 74% lymphocytes, and 2 young lymphocytes. The hematologist reported severe pancytopenia and hypocellular marrow with a few primitive cells, possibly representing early leukemic changes.

The report on the biopsy specimen was as follows: Epidermis was somewhat atrophic. Beneath this was a band of relatively normal connective tissue. Deeper was a cellular infiltrate composed of endothelial cells with numerous mitotic figures. There were many extravasated erythrocytes. No pigment was seen.

DISCUSSION

DR. DOUGLASS A. DECKER, Allentown: The following points are against the diagnosis of Kaposi's sarcoma: the rapidity with which the process developed, the unusual distribution, the fact that it started not on the legs but on the chest and shoulders, and the fact that it developed in a 72-year-old American-born man of Irish descent. I was impressed by the generalized lymphadenopathy and the blood count, which showed 3,100 white blood cells with 74 per cent lymphocytes. This is a lymphoblastoma, probably aleukemic leukemia.

DR. FRED D. WEIDMAN: All agree that the distribution is atypical.

DR. A. STRAUSS: I have seen Kaposi's sarcoma generalized to that extent.

DR. FRED D. WEIDMAN: Of course all of us saw the cayenne-pepper-like hemorrhages and the large suggilations in the larger lesions. The surface markings of the skin overlying even the largest tumefactions were normal; all of the thin, delicate lines of the skin were normal. In Kaposi's sarcoma there is hyperkeratosis amounting sometimes almost to verrucosity, and invariably there are acanthosis and hyperkeratosis. Perhaps from the clinical standpoint alone that would be the most significant point in distinguishing between Kaposi's sarcoma and one of the lymphoblastomas in the present case and might be remembered to advantage in future cases. In lymphoblastomas, except perhaps mycosis fungoides, the epidermis is atrophic, and that is the case here. I thought from the sections that it looked like a reticulosis. I am sure that a reticulum stain would bring it out more clearly than it shows in these very good hematoxylin sections. Kaposi's sarcoma is of the order of a hemangioendothelioma—that is, with the emphasis on the endothelial cells—plus lymphocytes. These cells appear to me to be reticulum cells and I am inclined, especially in view of the tremendous lymphocytosis this patient has, to think this a lymphoblastomatous condition and probably an example of aleukemic reticulosis. Aleukemic reticulosis is very likely to be hemorrhagic, almost as severely hemorrhagic as this. The same is true of monocytic leukemias. The lesions are likely to be slaty and dusky because of the hemorrhages. There are numerous mitotic figures, and of course these cases of aleukemic reticulosis do go on to sarcomatous change. So I think there are enough features here to justify a diagnosis of aleukemic reticulosis.

DR. ROBERT L. BRECKENRIDGE (by invitation): There was considerable discussion in our department as to just what the condition was; it lacks the fibrosis, unless it is a very early lesion, of Kaposi's sarcoma. I did think there were a few mitotic figures in our sections. The cells are rather large; the nuclei particularly do suggest that they are reticulum cells. There are a good number of capillaries throughout the section. Whether they represent neoplastic capillaries or a portion of the granulation tissue in the tumor, we do not know.

DR. FRED D. WEIDMAN: Histological study of a lymph node would be very informative.

"Atrophie blanche et ulcère de jambe." Presented by DR. JOHN F. WILSON.

E. R., a white woman aged 32, presented small depigmented atrophic areas on the sides of both ankles. At the borders the skin was pigmented and telangiectatic. One area showed a small ulceration. During the past year an eruption has developed on the sides of both ankles. The patient thought at first that she might have injured them by bumping them in walking, but later lesions appeared on the outer sides of the ankles. Some of these lesions have broken down and become ulcerated.

The report on the biopsy specimen was as follows: Sections through the piece of skin submitted displayed slight hyperkeratosis of the epithelial border. In addition, the epithelium

showed focal zones of rather striking intercellular edema with vesicle formation. Some of the latter contained scattered erythrocytes while others contained a few granulocytes and detached epithelial cells. In some sectors the vesicles appeared to split the epithelial layer into two distinct, almost equal, layers. There was a slight granulocytic infiltration just beneath the basal layer of the epithelium in some regions. The superficial corium displayed a rather striking vascular change. Most of the small arterioles showed a fibrinoid type of necrosis of the wall, some being somewhat eccentrically thickened, with scattered erythrocytes within the wall proper. A few of the vessels appeared to be completely obliterated, no lumen being visible. Only a few scattered granulocytes were present about the vessels, and we do not regard the histologic picture as suggesting periarteritis nodosa. Other capillaries appeared distended and engorged with erythrocytes, and there were a few scattered hemorrhages in the deeper levels of the corium.

The patient has been treated with x-ray therapy, without change.

DISCUSSION

DR. JOHN F. WILSON: No positive diagnosis could be made in this case. It did not fit in with anything else and, unfortunately, I could not produce a description of the microscopic picture in this dermatosis and hope for help from histologists tonight. These are nonelevated ulcerating lesions. They begin with a hemorrhagic appearance and gradually break down. The biopsy was done on an early lesion, about 10 days old. This name is simply the French descriptive term of the clinical appearance of the lesion. There was a similar case presented at the International Congress, in London, and I could not find anyone, including the French, who knew anything about it. Biopsy was not performed on the patient in London, but I think that those who were there will remember the case. The distribution in that patient was also around the ankles.

DR. JOSEPH V. KLAUDER: I think that those lesions are commonplace and that the French have exaggerated their importance (Gonin, R.: Atrophie blanche et ulcère de jambe à douleurs intolérables, *Ann. dermat. et syph.* **10**:633 [Nov.-Dec.] 1950, p. 633, with discussion and illustration of histologic picture, proliferating endarteritis). The name, after all, is only descriptive. As you know, this is an area where atrophy will be found at the site of a previous ulceration. These areas are fairly common, appear along with superficial varicosities, and are characterized by a small area of ulceration, which again is characterized by severe pain out of all proportion to the small area of ulceration. They retrogress with atrophy which is white. I have always visualized them as comparable to varicose ulcer. They are of practical importance because of the pain, which may keep the patient awake. A recent writer advised cauterizing the ulceration. I have always treated the lesions with supportive bandages, and eventually this little ulceration disappears, leaving a white atrophic spot. In my office I have seen a dozen or more of such cases. They always start as a small superficial varicosity, not deep, always around the ulcer.

DR. FRED D. WEIDMAN: Postvaricose ulceration with cicatrix?

DR. JOSEPH V. KLAUDER: Expressed in English, that is a good name for it.

DR. JOHN F. WILSON: Dr. Weidman, can you fit that microscopic picture into that of varicosities?

DR. FRED D. WEIDMAN: It depends on the stage of the lesion.

DR. JOHN F. WILSON: This biopsy was done on a lesion about 10 days old.

DR. FRED D. WEIDMAN: There might be fibrinoid degeneration in the walls of the blood vessel if there were sufficient toxic effects; these effects of course would have to come from degenerated tissue. I would have to see the section, which is not on exhibit tonight. It would all depend on the form which the fibrinoid degeneration took.

Acrodermatitis Perstans (Hallopeau). Presented by DR. JOHN F. WILSON.

V. I. E., a white man aged 60, presented an acute erythematous, edematous, and crusted eruption, with pustules and vesicles at the borders, on the fingertips of both hands. The right index finger was most severely involved. Several of the nails were distorted.

An eruption appeared on the fingertips of both hands in February, 1952.

The fasting blood sugar was 84 mg. per 100 cc. Culture showed Staphylococcus aureus with oxytetracycline ("terramycin") sensitivity. The fungous culture showed Candida albicans (Dr. Albert M. Klingman).

The patient was treated with x-rays, ultraviolet rays, oxytetracycline orally and oxytetracycline ointment locally. There has been only slight improvement.

DISCUSSION

DR. JOSEPH V. KLAUDER: I subscribe to the diagnosis. I think the practical question is how to treat this patient.

DR. FRED D. WEIDMAN: Is there not some question as to whether this is a case of dermatitis repens?

DR. JOHN F. WILSON: I think Crocker felt that his cases were different from Hallopeau's, the dermatitis having more tendency to extend to other areas, whereas in Hallopeau's cases it tended to stay in the same area. The lesions in Crocker's dermatitis extend at the border and heal in the old areas.

DR. JOSEPH V. KLAUDER: Infiltrate the lesions with procaine and destroy them with superficial electrodesiccation and see what happens.

DR. JOHN F. WILSON: That is worth a trial. The patient certainly cannot be much more incapacitated than at present.

DR. HERBERT LUSCOMBE: I thought the condition looked something like psoriasis.

DR. DOUGLASS A. DECKER, Allentown: I thought of psoriasis, too. There is usually a prompt response to antibiotic drugs in acrodermatitis.

DR. JOHN F. WILSON: Practically all of the distortion of the nail has come as a result of inflammatory reaction at the base of the nail.

Hereditary Hemorrhagic Telangiectasis. Presented by CAPTAIN WILLIAM N. NEW (MC), U.S.N., and COMMANDER G. ANDERSON (MC), U.S.N. (by invitation).

J. J. J., a white youth aged 18, presented numerous scattered telangiectasis over the scrotum, arms, legs, ears, and nasal mucosa, and one lesion in the left conjunctiva. There was a suggestion of "frog spawn" appearance of the sides of the tongue.

The patient is the fourth of thirteen siblings, all of whom are living and well. The mother is living and well. The father died of a heart attack in 1949. The patient's father, according to the patient, had the same disease as the patient. He first noted this disorder as a child of 10. Three years ago spontaneous bleeding from the scrotal lesions occurred.

The laboratory findings were as follows: The Rumpel-Leede test was negative. Bleeding time was 3 minutes; coagulation time was 3 minutes and 30 seconds. Complete blood tests revealed 14 gm. hemoglobin, 4,700,000 erythrocytes, 7,880 leukocytes, 38% neutrophiles, 61% lymphocytes, 1% eosinophiles, and 96,000 thrombocytes (platelets). Roentgenograms of the chest and of the skull were negative.

Several of the larger lesions on the scrotum have been desiccated.

DISCUSSION

DR. JOHN F. WILSON: I have no therapeutic suggestions, but I thought that the scrotal lesions were most interesting. They reminded me of angiokeratoma, yet the keratinous feature of angiokeratoma is missing.

DR. JOSEPH F. RICCHIUTI, Pottsville: In *The Journal of the American Medical Association* (Koch, H. J., Jr.; Escher, G. C., and Lewis, J. D.: Hormonal Management of Hereditary Hemorrhagic Telangiectasis, J. A. M. A. **149**:1376-1380 [Aug. 9] 1952) there appeared a short article describing the treatment of such conditions by estrogenic substances. Several patients were so treated, successfully.

DR. JOSEPH V. KLAUDER: I have treated a few patients with rutin with apparently good results. I think it is certainly worth a trial. I should think Dr. New would be interested first of

all in learning whether this man should be kept in the Service. Why treat him? I am inclined to subscribe to the diagnosis. It would be interesting to know how many times those scrotal lesions are associated with Osler's disease. Has it been reported what per cent of patients with Osler's disease have scrotal lesions?

CAPTAIN WILLIAM N. NEW (MC), U. S. N.: This youth is presented because of the fact that he has had frequent bleeding from the thin-walled blood vessels of the scrotum. The bleeding starts without warning, and there is marked itching after the bleeding has started. These lesions represent a condition which is more than just simple angiokeratoma, though maybe the two conditions can coexist. Some of those lesions are so pale they might be hemangiolymphatic. Certainly the sides of the tongue have lesions which resemble circumscribed lymphangioma, frog-spawn type, and the soft palate is speckled with multitudinous frog-spawn accumulations.

DR. THOMAS BUTTERWORTH, Reading: These telangiectases can occur along the intestinal tract. About 1926, Dr. Napoleon Boston described a man who bled to death from such a lesion in the stomach.

DR. HERBERT LUSCOMBE: I saw such a case recently. The patient had acute intestinal hemorrhages, and, after the third of these, she died.

DR. JOSEPH V. KLAUDER: Hemorrhagic telangiectasia was described prior to Fordyce. Herman Beerman has made me historically minded since he asked me to lecture on the historical aspects of dermatology. According to Crocker, the disease was first described by Cottle. Colcott Fox was also one of the first to describe the disease, under the name of lymphangiectasis. Its present name was given to it by Mibelli in 1889.

DR. HENRY B. DECKER, Camden, N. J.: I have seen hemorrhages from angiokeratoma due to trauma. One of the interesting things about Osler's disease is that it occurs frequently in pregnancy. I have one patient who has had three children, and each time during pregnancy these lesions break out and after delivery the condition subsides.

DR. FRED D. WEIDMAN: Does anyone think that this might be lymphangioma circumscriptum?

DR. JOSEPH V. KLAUDER: It looks entirely different from that. It lacks the white cystic vesicles that characterize that condition. These are purplish-red puncta.

DR. THOMAS BUTTERWORTH, Reading: The frog-spawn appearance is very common among the feebleminded. Lesions of this type which I have removed have been reported by the histologist as lymphangioma circumscriptum. This feature is not very pronounced in this case, though there were a few lesions present that suggested that diagnosis.

DR. FRED D. WEIDMAN: It appears from this case that there is a hereditary weakness of the blood vascular structures as well as of the lymphatic ones.

Erythema Elevatum Diutinum (Eosinophilic Granuloma Type). Presented by DR. JOHN F. WILSON.

J. O'D., a white man aged 32, presented on the left side of the forehead a number of purplish elevated infiltrated plaques, which had become confluent. There were two similar lesions of the left cheek. During the past several years purplish lesions have developed on the forehead and the left cheek. They have increased in size gradually.

The report on the biopsy specimen was as follows: The small piece of tissue submitted was bordered by a normal zone of stratified squamous epithelium overlaid by a slight amount of keratin. Beneath the epithelium there was a zone of normal-appearing corium, directly beneath which were well-circumscribed granulomatous infiltrations. The latter were composed of granulocytes, eosinophiles, scattered lymphocytes, and macrophages. The cells showed no definite arrangement about skin appendages. The vascular elements were moderately prominent and engorged.

Since June 13, 1952, there has been definitely a slow and gradual involution of all the lesions under treatment with antihistaminics and zinc oxide paste.

DISCUSSION

DR. FRED D. WEIDMAN: There are a few eosinophiles in the sections exhibited tonight and a few polymorphonuclears and histiocytes. The walls of the blood vessels do not show any

fibrinoid degeneration of the capillary walls. The walls are edematous and appear unduly fibrillar. I always dislike to diagnose erythema elevatum diutinum—and Ketron is of the same mind—unless fibrinoid degeneration of the vessel walls is found. However, I do not think that we ought to insist too strictly on adherence to a histologic picture. That is bound to vary in different stages of the disease. I judge that the histologic picture here is not indicative of erythema elevatum diutinum. It is compatible with eosinophilic granuloma of the face with eosinophilia.

DR. A. STRAUSS: This is a very hard case to discuss under this diagnosis because I do not believe that our members have seen many cases of so-called erythema elevatum diutinum. But the two which I have seen did not look like this at all. The lesions were more infiltrated, browner, thicker, and more widespread and there were many concomitant symptoms—joint symptoms, and so on. Whether this is an entity in itself or a different phase of some other disease, I do not think it is very easily diagnosed, because when I looked it up there were very few cases reported in the literature.

DR. FRED D. WEIDMAN: Clinically, I would not think for a moment of erythema elevatum diutinum. In studying the sections one does have to distinguish erythema elevatum diutinum from the granuloma of the face with eosinophilia. Lymphocytoma cutis is "out." I think that the diagnosis is "granuloma of the face with eosinophilia," of the erythema elevatum diutinum type histologically.

Fixed Drug Eruption from Trimethadione (Tridione®). Presented by DR. JOHN F. WILSON.

Drug Eruption from Mercuric Compounds. Presented by DR. HENRY B. DECKER and DR. HERBERT LUSCOMBE.

Multiple Benign Cystic Epithelioma Vs. Basal Cell Carcinoma. Presented by DR. HERBERT LUSCOMBE and (by invitation) DR. J. K. CORSON.

Macular Atrophy. Presented by DR. JOSEPH F. RICCHIUTI, Pottsville.

Subacute Lupus Erythematosus with Prompt Recovery. Presented by DR. JOSEPH V. KLAUDER.

1. Pityriasis Rubra Pilaris. 2. Psoriasis—Precipitating Factor Solar Dermatitis. 3. Generalized Lichen Planus. Presented by DR. HENRY H. PERLMAN.

Directory of Dermatologic Societies *

INTERNATIONAL

International Congress of Dermatology and Syphilology

Guido Meischer, Chairman, International Committee, Zurich, Switzerland.
Sven Hellerström, Secretary, International Committee, Stockholm, Sweden.
Place: Stockholm. Time: 1957.

Pan American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Joseph J. Eller, President, 745 Fifth Ave., New York 22.
John G. Downing, Secretary, 520 Commonwealth Ave., Boston.
Place: Floating Medical Congress S.S. *Nieu Amsterdam* visiting Carribean Countries. Time: January 7-19, 1953.

FOREIGN

The British Association of Dermatology

J. E. M. Wigley, President, 132, Harley St., London, W.1.
G. B. Dowling, Secretary, 24, Wimpole St., London, W.1.

British Association of Dermatology and Syphilology (New South Wales Branch)

W. K. Myers, President, 135 Macquarie St., Sydney, Australia.
A. G. Finley, Secretary, 335 Macquarie St., Sydney, Australia.
Place: Royal North Shore Hospital, St. Vincent's Hospital, Sydney Hospital, Lewisham Hospital, Royal Prince Alfred Hospital, Royal Alexandra Hospital for Children, and Royal Newcastle Hospital. Time: 4:00 p.m., on Fridays, approximately every two months.

Canadian Dermatological Association

G. Brock, President, 413 Medical Arts Bldg., Winnipeg, Man.
A. Birt, Secretary, 429 Medical Arts Bldg., Winnipeg, Man.
Place: Winnipeg. Time: 1953.

Dermatological Association of Australia

M. R. Healy, President, 110 Collins St., Melbourne.
R. F. A. Becke, Secretary, 139 Macquarie St., Sydney.
Place: Adelaide. Time: 1953.

German Society of Dermatology

Alfred Marchionini, Chairman, Dermatological Clinic, University of München.
Otto Grütz, Secretary, Dermatological Clinic, University of Bonn.

Israeli Dermatological Society

A. Dostrovsky, Chairman, Hebrew University Hadassah Medical School, Jerusalem.
Felix Sagher, Secretary, Hebrew University Hadassah Medical School, Jerusalem.

*Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

New Zealand Dermatological Society

H. W. Wilson, President, Lister Bldg., Victoria St. E., Auckland, C.1.
R. G. Park, Secretary, Kelvin Chambers, 16 The Terrace, Wellington. C.1.

North British Dermatological Society

President: Senior dermatologist in city where meeting is held.
P. W. Hannay, Honorary Secretary, 22 Nile Grove, Edinburgh 10, Scotland.

Royal Society of Medicine, Section of Dermatology

G. B. Dowling, President, 24, Wimpole St., London, W.1.
D. I. Williams and H. E. Vickers, Secretaries, 1, Wimpole St., London, W.1.
Place: Royal Society of Medicine, 1 Wimpole St., London, W.1. Time: 4:00 p.m., third Thursday of each month.

Sociedad Mexicana de Dermatologia

Silvestre Rico, Chairman.
Fernando Latapi, Secretary, Zacatecas 220-6, México, D. F.
Place: National School of Medicine, México, D. F. Time: 9:00 p.m., first Thursday of each month.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

John H. Lamb, Chairman, 705 Medical Arts Building, Oklahoma City 2.
J. Walter Wilson, Secretary, 3875 Wilshire Blvd., Los Angeles 5.
Place: New York. Time: June 1-5, 1953.

American Academy of Dermatology and Syphilology

Michael H. Ebert, President, 55 E. Washington St., Chicago 2.
John E. Rauschkolb, Secretary, 25 Prospect Ave., N.W., Cleveland 15.
Place: Palmer House, Chicago. Time: Dec. 5-10, 1953.

American Board of Dermatology and Syphilology

Anthony C. Cipollaro, President, 40 E. 61st St., New York 21.
George M. Lewis, Secretary, 66 E. 66th St., New York 21.

American Dermatological Association

Earl D. Osborne, President, 71 North St., Buffalo 2.
Louis A. Brunsting, Secretary, 102 Second Ave. S.W., Rochester, Minn.
Place: The Lake Placid Club, Essex County, New York. Time: June 9-13, 1953.

Society for Investigative Dermatology

Theodore Cornbleet, President, 30 N. Michigan Ave., Chicago 2.
Herman Beerman, Secretary, 255 S. 17th St., Philadelphia 3.
Place: New York. Time: May 30-31, 1953.

SECTIONAL

Central States Dermatological Association

Marvin Winer, President, 333 Linwood Ave., Buffalo 9.
Frank A. Dolce, Secretary, 568 Delaware Ave., Buffalo 2.

New England Dermatological Society

Joseph Goodman, Secretary, 375 Commonwealth Ave., Boston.

Place: New Haven Hospital, New Haven, Conn., and Massachusetts General and Boston City hospitals (in alternation), Boston.

Pacific Dermatologic Association

Norman N. Epstein, President, 450 Sutter St., San Francisco.

Ervin Epstein, Secretary, 447 29th St., Oakland, Calif.

Place: Seattle, Wash., Olympic Hotel. Time: July, 1953.

Pacific Northwest Dermatological Society

Sam E. Light, President, Medical Arts Bldg., Tacoma, Wash.

Leon F. Ray, Secretary, 628 Medical Dental Bldg., Portland 5, Ore.

Place: Place varies. Time: Third Thursday of May and October.

Rocky Mountain Dermatologic Society

Gerald M. Frumess, President, 2200 E. 18th Ave., Denver.

Thomas W. Moffatt, Secretary, 822 Majestic Bldg., Denver.

Place: Selected prior to each meeting. Time: Selected prior to each meeting.

Southern Dermatological Association

C. A. Andrews, Chairman, 706 Franklin St., Tampa, Fla.

Joseph Farrington, Secretary, 204 Laura St., Jacksonville, Fla.

Southern Medical Association, Section on Dermatology and Syphilology

D. Truett Gandy, President, 424 Medical Arts Building, Houston 2, Texas.

Ray O. Noojin, Secretary, 620 S. 20th St., Birmingham, Ala.

Southwestern Dermatological Society

Samuel J. Jelso, President, Medical Arts Square, Albuquerque, N. M.

Robert H. Snapp, Secretary, 15 E. Monroe, Phoenix, Ariz.

Place: Various cities in Arizona, New Mexico, and Western Texas, in the fall; In conjunction with meeting of Rocky Mountain Dermatological Society, in the spring. Time: Fall and spring.

STATE

Alabama Dermatologic Society

William L. Poole, President, Woodward Building, Birmingham.

Irvind D. London, Secretary, 746 Adams Ave., Montgomery.

Arkansas Dermatological Society

Davis W. Goldstein, Chairman, Cooper Clinic, Fort Smith.

Ray Fulmer, Secretary, 103 E. Seventh St., Little Rock.

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Rees B. Rees, Chairman, 380 Post St., San Francisco.

Frances M. Keddie, Secretary, 300 Homer Ave., Palo Alto.

Connecticut State Medical Society, Section on Dermatology

Joseph Becker, Chairman, 302 State St., New London.
Jack J. Albom, Secretary, 43 Trumbull St., New Haven.
Place: New Haven.

Florida Society of Dermatology and Syphilology

Lewis Capland, President, 350 Lincoln Road, Miami Beach 1.
Morris Waisman, Secretary, 1201 Citizens Bldg., Tampa 2.

Hawaii Dermatological Society

Harry L. Arnold, Jr., Secretary, 881 S. Hotel St., Honolulu 53.

Indiana State Dermatological Society

Daniel Tweedal, President, 527 Sycamore St., Evansville.
Robert E. Jenkins, Secretary, 3311 N. Meridian, Indianapolis 8.

Louisiana Dermatologic Society

Lee McLean, Chairman, Pere Marquette Bldg., New Orleans.
F. C. Grieshaber, Secretary, Pere Marquette Bldg., New Orleans.
Place: Louisiana State Charity Hospital, New Orleans. Time: Third Sunday of each month.

Massachusetts Medical Society,
Section on Dermatology and Syphilology

Ethel M. Rockwood, President, 416 Marlboro St., Boston 15.
S. J. Messina, Secretary, 520 Commonwealth Ave., Boston 15.
Place: Hotel Statler, Boston.

Medical Society of the State of New York,
Section on Dermatology and Syphilology

George M. Lewis, President, 66 E. 66th St., New York 21.
Frank A. Dolce, Secretary, 468 Delaware Ave., Buffalo.

Michigan State Medical Society
Section on Dermatology and Syphilology

J. R. Delaney, Chairman, 1020 David Whitney Bldg., Detroit 26.
C. J. Courville, Secretary, 1202 Maccabees Bldg., Detroit 2.

Minnesota Dermatological Society

Elmer T. Ceder, President, 511 Medical Arts Bldg., Minneapolis 2.
Harold G. Ravits, Secretary, 546 Lowry Medical Arts Bldg., St. Paul.

New Jersey Dermatological Society

Eva T. Brodkin, President, Newark.
Frederick C. Licks, Secretary, 64 Scotland Road, South Orange.

Oklahoma Dermatological Association

Hervey A. Foerster, President, 1200 N. Walker, Oklahoma City.
Robert J. Morgan, Secretary, 1111 N. Lee, Oklahoma City.
Place: Oklahoma City and Tulsa, alternately. Time: Annually, in the spring.

RHODE ISLAND DERMATOLOGICAL SOCIETY

Carl D. Sawyer, President, 184 Waterman St., Providence.
Malcolm Winkler, Secretary, 199 Thayer St., Providence.

TEXAS DERMATOLOGICAL SOCIETY

C. H. McCuistion, President, 609 Capital National Bank Bldg., Austin.
Thomas L. Shields, Secretary, 1216 Pennsylvania Ave., Fort Worth.
Place: Rotating. Time: Spring, coincident with Texas State Medical Association; fall, October.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

James Q. Gant, Jr., Chairman, 1726 M St., N.W., Washington, D. C.
Jack L. Derzavis, Secretary, 1835 Eye St., N.W., Washington, D. C.
Place: Baltimore and Washington. Time: Third Thursday of each month, in alternate cities, October to May.

BRONX DERMATOLOGICAL SOCIETY

Rudolf L. Baer, President, 962 Park Ave., New York.
Henry Silver, Secretary, 290 W. End Ave., New York.
Place: Academy of Medicine. Time: Third Thursday of every month, October to May.

BROOKLYN DERMATOLOGICAL SOCIETY

Samuel I. Greenberg, President, 277 Eastern Parkway.
Harry L. Feigenbaum, Secretary, 352 77th St.
Place: Brooklyn Hospital Clinic, Ashland Place and DeKalb Ave. Time: Third Monday of each month, October to May.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Marvin Winer, President, 333 Linwood Ave., Buffalo.
Frank A. Dolce, Secretary, 468 Delaware Ave., Buffalo.
Place: Edward J. Meyer Memorial Hospital, Buffalo, and Strong Memorial Hospital, Rochester. Time: Second Tuesday of every month, October to May, inclusive.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Joseph J. Russo, President, 736 Madison Ave., Albany.
Frank Fagan, Secretary, 65 Second St., Troy.

CHICAGO DERMATOLOGICAL SOCIETY

James R. Webster, President, 55 E. Washington St. (2).
John M. McCuskey, Secretary, 331 Fulton St., Peoria, Ill.
Place: Chicago. Time: Third Wednesday of each month except June, July, August, and September.

CINCINNATI SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

Harry A. Nieman, President, 570 Fidelity Bldg., Dayton, Ohio.
Raymond R. Suskind, Secretary, Kettering Laboratory, University of Cincinnati, Cincinnati.
Place: Cincinnati General Hospital. Time: 8:00 p. m., first Wednesday of each month, October to May.

CLEVELAND DERMATOLOGICAL SOCIETY

George H. Curtis, President, Cleveland Clinic (6).
John R. Haserick, Secretary, Cleveland Clinic (6).

Dallas Dermatological Society

Bedford Shelmire, President, 1410 Medical Arts Bldg.
D. Shelton Blair, Secretary, 304 Medical Arts Bldg.
Place: Medical Arts Bldg. Time: Third Wednesday of each month.

Detroit Dermatological Society

Chester A. Doty, President, 1735 David Whitney Bldg. (26).
Henry A. Brunsting, President-Elect, 2001 Collingwood Ave., Toledo, O.
Charles J. Courville, Secretary, 1202 Maccabees Bldg. (2).

Kansas City Dermatological Society

Thomas B. Hall, President, 902 Professional Bldg., Kansas City 6, Mo.
Bernard H. Winston, Secretary, 324 Professional Bldg., Kansas City 6, Mo.
Place: University of Kansas Medical Center, Kansas City, Kan. Time: 10:00 a. m., second Sunday of each month, from October through June.

Long Island Dermatological Society

Charles S. Miller, President, Corona, N. Y.
Conrad Stritzler, Secretary, 90-26 148th St., Jamaica 2, N. Y.
Place: Queens General Hospital, Jamaica, N. Y. Time: Second Tuesday of each month, 8:00 p. m.

Los Angeles Dermatological Society

Stanton B. May, President, 119 N. Central Ave., Glendale, Calif.
Irving A. Lewe, Secretary-Treasurer, 3319 W. Beverly Blvd., Montebello, Calif.
Place: Good Hope Clinical Association. Time: Second Tuesday of each month, October to May.

Manhattan Dermatologic Society

Samuel M. Peck, President, 33 E. 70th St. (21).
George M. Lewis, Secretary, 66 E. 66th St. (21).
Place: Each member's office, in rotation. Time: 8:00 p. m., second Tuesday of each month.

Metropolitan Dermatological Society

Joseph C. Amersbach, President, 105 E. 53rd St., New York.
Valentine C. Baker, Secretary, 619 W. 140th St., New York.
Place: Offices of members. Time: Third Monday of each month, October to May.

Metropolitan Dermatological Society of Chicago

I. M. Corbin, President, 108 Scott St., Joliet, Ill.
T. Benedek, Secretary, 25 E. Washington St., Chicago 2.
Place: Chicago, alternating in the Services of the Fellows. Time: Second Wednesday, 10:00 a. m., from October to May.

Metropolitan Dermatological Society of Los Angeles

Harold C. Fishman, President, 105 N. San Vicente Blvd., Beverly Hills, Calif.
Fred F. Feldman, Secretary, 6333 Wilshire Blvd., Los Angeles.
Time: Fourth Tuesday of each month, October through May.

Milwaukee Dermatologic Society

M. J. Reuter, President, 324 E. Wisconsin Ave.
Donald M. Ruch, Secretary, 208 E. Wisconsin Ave.

Montreal Dermatological Society

Frederick Kalz, President, 1414 Drummond St.

B. P. Heller, Secretary, 1538 Sherbrooke St., W.

Place: Royal Victoria Hospital, Notre Dame Hospital, Montreal General Hospital, and other hospitals. Time: October, February, and April.

New York Academy of Medicine, Section of Dermatology and Syphilis

Anthony C. Cipollaro, Chairman, 40 E. 61st St. (21).

J. Lowery Miller, Secretary, 371 Park Ave.

Place: New York Academy of Medicine, 2 E. 103rd St. Time: First Tuesday of each month.

New York Dermatological Society

Anthony C. Cipollaro, Chairman, 40 E. 61st St. (21).

Maurice J. Costello, Secretary, 140 E. 54th St.

Place: New York. Time: Fourth Tuesday of each month.

Omaha Dermatological Society

Olin J. Cameron, President, 1520 Medical Arts Bldg.

George F. Pinne, Secretary, 453 Aquila Ct.

Philadelphia Dermatological Society

Fred D. Weidman, Chairman, Medical Laboratories, University of Pennsylvania. (4).

Bertram Shaffer, Secretary, 1820 Pine St. (3).

Place: Philadelphia hospitals. Time: Third Friday of each month except June, July, and August.

Pittsburgh Dermatological Society

Samuel R. Perrin, President, 119 S. Highland Ave. (6).

William B. Guy, Secretary, 7026 Jenkins Arcade.

Place: Falk Clinic, 3601 Fifth Ave. Time: Third Thursday of each month.

San Francisco Dermatological Society

Rees B. Rees, President, 384 Post St.

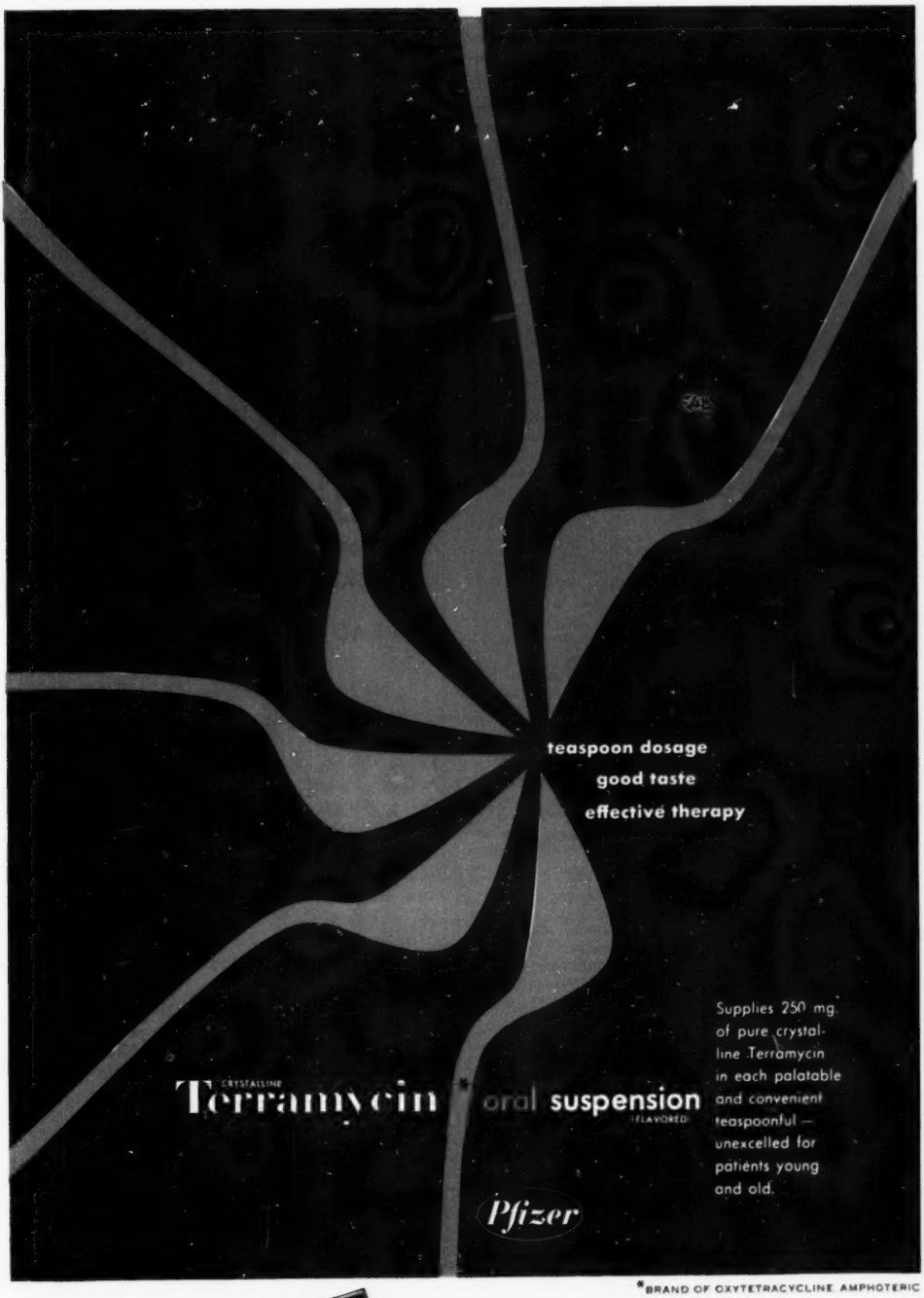
Max Krause, Secretary, 400 59th St., Oakland 9.

St. Louis Dermatological Society

Joseph Grindon Jr., President, 539 N. Grand Ave. (3).

Morris Moore, Secretary, 3427 Washington Blvd.

Place: Barnard Free Skin and Cancer Hospital. Time: 8:00 p. m., third Monday of each month, October to May.



*BRAND OF OXYTETRACYCLINE AMPHOTERIC

DON'T MISS APPEARING REGULARLY IN THE J. A. M. A.

CROLEUM

TRADE MARK REG. U. S. PAT. OFF.

suspensoid vehicle

What It is . . .

CROLEUM SUSPENSOID VEHICLE is a colloidal emulsion used to compound topical applicant prescriptions and as a non-irritating dermal emollient without added medication. It has the following characteristics:

Creamy, opaque, white semi-fluid—flows readily. Dispersible in water or aqueous body exudates. Spreads instantly on wet or dry treated areas. Non-irritating, non-staining, non-drying. Penetrates actively into tiny dermal crevices. Easy to apply—pour, swab, spread or spray. Excellent dermal emollient and massage lubricant. Compatible with most used topical drugs. Forms no impenetrable grease films. Pleasant odor, pH 6.6-6.8

What It Is For . . .

CROLEUM Vehicle is an excellent base in which to compound prescribed topical drugs. Pour desired quantity of CROLEUM Vehicle into glass or porcelain mortar and blend in the prescribed medications with pestle (non-metallic). CROLEUM Vehicle will dissolve aqueous or oil soluble drugs. Insoluble drugs or amounts in excess of saturation level will remain suspended in the carrier over wide temperature variations.

CROLEUM Vehicle without added medication is an excellent non-irritating, low cost, dermal emollient and detergent. It finds many hospital uses as an effective massage lubricant, skin cleanser and general purpose skin lotion. Dilute with distilled water if thinner consistency is desired.

How Administered . . .

CROLEUM is non-drying and flows readily. Apply to skin with spray, swab or sponge—flow it on—spread with sterile tongue blade—or dilute with sterile distilled water (50%) and spray. Use also as a wet dressing or pack. Dressings will seldom adhere to CROLEUM treated surfaces.

What It Does . . .

While this is determined by the added medicament and its strength, CROLEUM prepared prescriptions of low drug concentration may produce therapeutic results not surpassed by larger amounts in ordinary grease bases. No grease films are formed. CROLEUM with added medication actively penetrates incrustations and small dermal crevices and thus provides intimate medication contact in otherwise inaccessible places.

14 Years of Successful Use

Chester-Kent, Inc.
100 S. Wabasha, St. Paul 1, Minn.

ACCEPTED
COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION
AMERICAN MEDICAL ASSOCIATION

NOW

COUNCIL ACCEPTED

DOME-PASTE BANDAGE

A 4 inch by 10 yard IMPROVED Unna's Paste Boot

READY FOR IMMEDIATE USE

NO PRELIMINARY HEATING REQUIRED

EASILY APPLIED

Remains fresh and soft indefinitely, because it is packed in a special airtight container.

Indicated for the effective treatment of

VARICOSE ULCERS

DOME CHEMICALS INC.
109 West 64th Street New York 23, N. Y.

NEW

prescription

product

for Seborrheic Dermatitis of the Scalp

. . . itching, scaling Completely Controlled

in majority of cases

• Now, after years of research, an outstanding new treatment for seborrheic dermatitis of the scalp . . . SELSUN Sulfide Suspension. Its advantages: truly effective control of scaling; prompt, often immediate, relief of itching and burning; marked simplicity of use; wide range of effectiveness, from simple dandruff to severe seborrheic dermatitis. Plus the fact that SELSUN is promoted ethically, and is supplied *only on a physician's prescription.*

• Optimum results are obtained in four to eight weeks, after which control of symptoms is maintained for one to four weeks with each application. Itching and burning usually stop after the first two or three applications. Clinical investigators[1,3] treated 400 patients with SELSUN, reported *complete control* in 92 to 95 percent of cases of common dandruff, and 81 to 87 percent of all cases of seborrheic dermatitis. Many cases had failed to respond to other methods of treatment.

• Convenient to use, SELSUN is simply applied while washing the hair, then rinsed out. No messy ointments. No complicated application and removal procedures. Leaves scalp clean, odorless and with no residue to stain linens. Toxicity studies[1,2] showed SELSUN to have no ill effects when used externally as recommended. SELSUN is available at pharmacies in 4-fluidounce bottles. Why not give it a trial? Abbott

PRESCRIBE

SELSUN

TRADE MARK

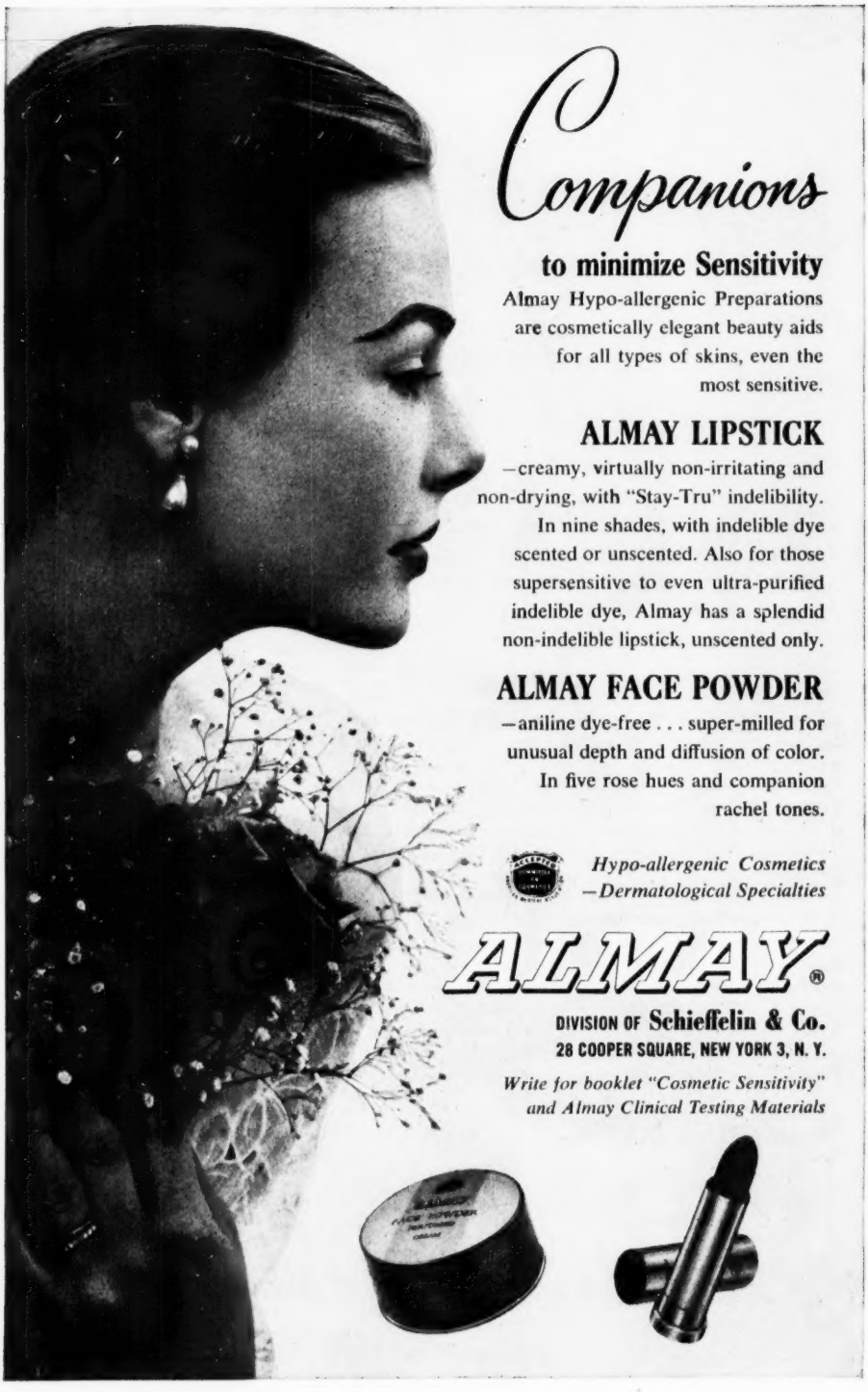
SULFIDE Suspension

(*Selenium Sulfide, Abbott*)

REFERENCES:

1. Slinger, W. N., and Hubbard, D. M. (1951), Arch Dermat. & Syph., 64:41, July.
2. Slepyan, A. H. (1952), *Ibid.*, 65:228, February.
3. Ruch, D. M. (1951), Communication to Abbott Laboratories.

1-95



Companions

to minimize Sensitivity

Almay Hypo-allergenic Preparations are cosmetically elegant beauty aids for all types of skins, even the most sensitive.

ALMAY LIPSTICK

—creamy, virtually non-irritating and non-drying, with "Stay-Tru" indelibility. In nine shades, with indelible dye scented or unscented. Also for those supersensitive to even ultra-purified indelible dye, Almay has a splendid non-indelible lipstick, unscented only.

ALMAY FACE POWDER

—aniline dye-free . . . super-milled for unusual depth and diffusion of color. In five rose hues and companion rachel tones.

Hypo-allergenic Cosmetics
—Dermatological Specialties

ALMAY®

DIVISION OF **Schieffelin & Co.**
28 COOPER SQUARE, NEW YORK 3, N. Y.

Write for booklet "Cosmetic Sensitivity" and Almay Clinical Testing Materials

g.s. DERMABASE
A greaseless, non-staining cream . . . easily removed with water, even from hairy parts . . . as acceptable as a cosmetic to patients.
g.s. DERMABASE
Compatible with an unusually wide range of both oil and water soluble drugs.
g.s. DERMABASE
NEW ALL-PURPOSE HYPO-ALLERGENIC OINTMENT BASE
g.s. DERMABASE
The pH is close to the pH of normal skin, which helps preserve the acid mantle of the skin.
CHICAGO 47, ILL.
Marcelle®
PHARMACEUTICALS
Division of Marcelle Cosmetics Inc.

Pleasingly and efficiently
serving patient and physician
during all seasons

SUPERFATTED

BASIS* SOAP

*Trade mark

For dry sensitive skin

Available at Prescription Pharmacies

DUKE LABORATORIES, INC
STAMFORD, CONN., U. S. A.

Mfgrs. of Aquaphor—Elastoplast, Trade marks

Limited Edition *Ready March 1953*

NOTABLE CONTRIBUTORS to the
KNOWLEDGE OF DERMATOLOGY

By Herman Goodman, M.D.

A recital of 5000 years of progress in Dermatology with pertinent references to basic sciences. Complete with biographical data covering approximately 1200 persons, departed, or if living, more than 70 years of age.

A BOOK FOR YOUR PLEASURE AND PROFIT!

Limited Printing—Avoid Disappointment—Order Now!

ORDER FORM

Medical Lay Press
18 E. 89 St., Dept. ADS
New York City 28, N. Y., USA

Enclosed please find my check for ten dollars. I expect a copy of NOTABLE CONTRIBUTORS TO THE KNOWLEDGE OF DERMATOLOGY about March 1953. I retain the privilege of returning the book within ten days of its receipt if unsatisfactory for any reason.

NAME .....
(PLEASE PRINT)

ADDRESS .....

CITY..... ZONE..... STATE.....

For a clean scalp..

YOU HAVE undoubtedly told many of your patients that a clean scalp is as important as clean hands . . . that a healthy scalp has much to do with a healthy skin, particularly the skin of the face.

Perhaps you have recommended the use of Packers Tar Soap. As a gentle, pleasant and dependable cleansing agent for the scalp and hair, Packers has won the approval of many dermatologists.

Packers also offers the advantage of economy. Shampoos with this famous cake soap average less than a penny—about one-fourth the cost of bottled shampoos.

PACKERS TAR SOAP, INC.
MYSTIC, CONNECTICUT

MARCELLE FOUNDATION LOTION FOR OILY SKIN, in three different shades, is an excellent cosmetic vehicle for sulfur, resorcinol and other medicaments. Used alone, it is an effective drying lotion with astringent and protective properties . . . and entirely free from oils, fats and waxes.

The morale of acne patients is greatly improved with Marcelle Foundation Lotion for Oily Skin. The delicate mat finish camouflages cutaneous blemishes and remains flawless for hours. The choice of three shades — light, medium and dark — assures accurate blending with the skin coloring. Available in 2 oz. bottles. Write for professional samples.

The first line of cosmetics accepted by the Committee on Cosmetics of the A. M. A.

ACCEPTED COMMITTEE ON COSMETICS

MARCELLE COSMETICS, INC.
1741 North Western Ave.
Chicago 47, Illinois

Marcelle
HYPO ALLERGENIC
COSMETICS

COSMETICS FOR SENSITIVE AND ALLERGENIC SKINS

It Cleans Without Offense

Four ounce jar $1.50

CREAM OF SOAP (red label) the colloidal skin cleanser is mild and gentle, cleans without offense. It cleans by adsorption without hydrolizing or the release of free alkali. Massaged lightly on the unwetted skin, then rinsed with luke-warm water, it cleans without excessive degreasing action or drying; leaves the skin comfortable. It has been found of value in the management of sensitive skins with normal or excess oiliness, and as an adjunct to treatment.

A full sized jar for your personal use gladly sent on request.

PERSONAL LUXURIES, INC., Newtown, Penna.

For patients requiring hand protection—

Waterproof, CLOTH-LINED RUBBER GLOVES

Excellent protection where *dishwashing, laundering, cleaning, dusting, painting, gardening, etc.,* may cause dermatitis or intensify skin disorders.

Soft *cotton-lining* absorbs perspiration, prevents contact with rubber, makes gloves slip on and off easily.

Easy to work in, light and pliable. Long cuffs protect wrists. Women *like* wearing them!

For women: Small, medium and large sizes.

Clip this advertisement as your reminder to prescribe or order.

$9 a dozen pairs, $1.25 a pair postpaid

JANET FORISTER Dept. 124
Bloomington, Illinois

BOOKLETS ON MENTAL HYGIENE

Here are several booklets on mental hygiene that may prove of interest and use to you and your patients.

EMOTIONAL HEALTH IN WORK AND PLAY. T. R. Retlaw. 8 pages. 15 cents.

MEETING EMOTIONAL DEPRESSION. Franz Alexander. 16 pages. 15 cents.

REPORT OF A.M.A. COMMITTEE ON MENTAL HEALTH. 48 pages. 15 cents.

MESMERISM MINUS MESMER. Stefan Zweig. A discussion of hypnotism. 5 pages. 5 cents.

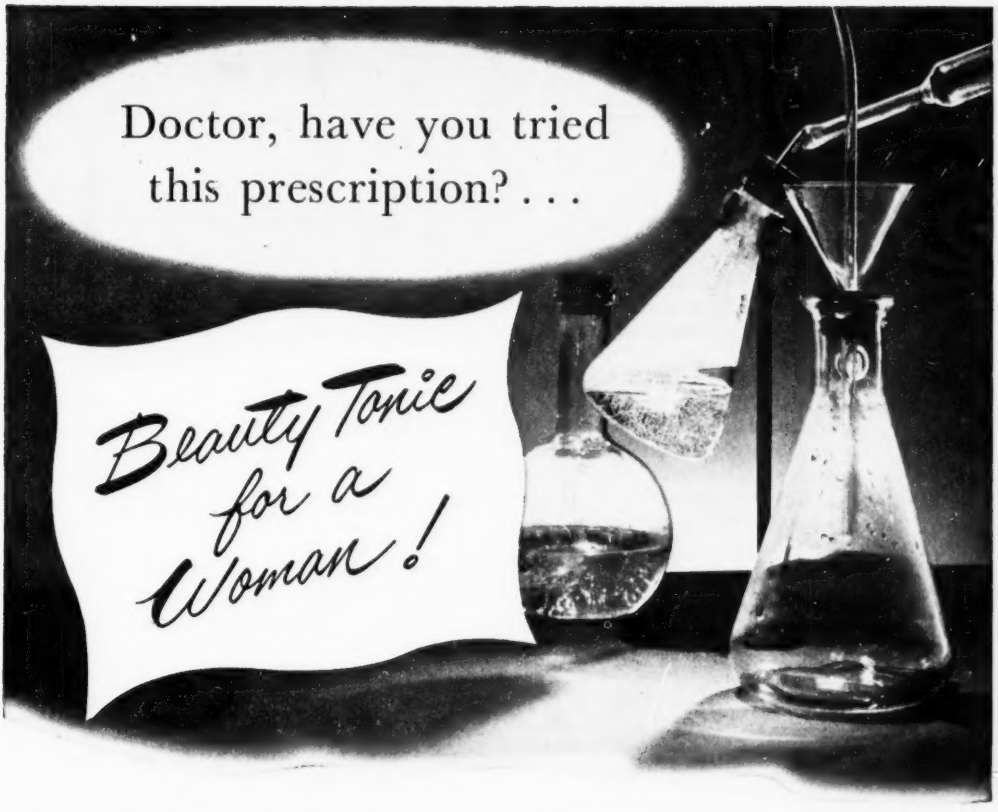
NERVOUSNESS. Isidore Margaretten. 4 pages. 5 cents.

THE TYRANNY OF NERVES. Edline Church Dubois. 3 pages. 5 cents.

SHOCK THERAPY SAVES MINDS. Harold Shryock. 5 pages. 5 cents.

Keep a supply of these booklets on hand. Available at lower cost for quantity purchases.

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn Street
Chicago 10, Illinois



We realize that countless times your patients ask you about the cosmetics they should use. If you are not already familiar with Beauty Counselor products, we would like you to know about them.

There are several other fine, hypo-allergenic skin care and make-up preparations on the market today, but Beauty Counselors is the *only* company offering a complete "Try-Before-You-Buy" service that assures our clients they are getting the most effective make-up and the correct creams and lotions for their particular types of skin.

Let us send you our confidential formulas so you may be the judge of their purity and efficacy. Better still, let us also send a trained Beauty Counselor to demonstrate our products to your wife in the privacy of her own home. There is no obligation for this service, of course.

Just mail the coupon below.

IT'S TRIAL AND NO ERROR WITH

Beauty Counselors

Grosse Pointe, Michigan • London, England • Windsor, Canada

BEAUTY COUNSELORS, INC.
Grosse Pointe, Michigan

☐ Please send me your qualitative formulas.

☐ Arrange to give my wife a demonstration of your products at no obligation.

Dr. _____

Office Address _____

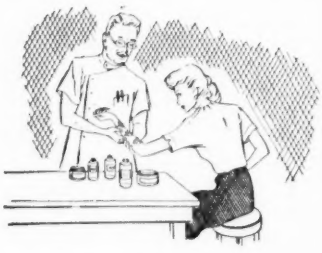
Home Address _____

City _____ Zone ____ State _____

Luzier's Service In The Field Of Allergy

When patient has history of cosmetic sensitivity, or when cosmetics may reasonably be suspected as a contributing if not the etiological factor in your patient's symptoms of allergy, we suggest:

1) Primary tests with those of our products your patient is using or contemplates using, to eliminate products to which there is no demonstrable reaction. (We suggest patch testing because it simulates normal conditions of use. The inside of forearm is good field for these tests.)



2) Secondary tests with constituents of products causing reaction, to trace offending agents. (In specific cases, on written request, we supply testing materials, gratis.)

3) Modification of formulae, when possible, to eliminate ingredients to which patient demonstrated a sensitivity. (We extend this service to our patrons without extra charge.)

4) Final check tests with modified formulae to make certain there is no reaction.

Preparations by Luzier are regularly available in an unscented variation. They do not contain orris root or rice starch. Any of their normally harmless constituents, however, is potentially allergenic, for which reason we suggest testing, when practicable. Fees for such tests are patient's responsibility.

LUZIER'S, INC., MAKERS OF FINE COSMETICS . . KANSAS CITY 3, MO.

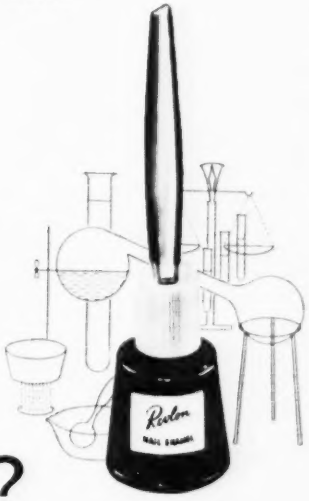
Did you know that...

ONE:

more women wear Revlon than any other nail enamel in the world

TWO:

Revlon is used professionally in over 95% of America's beauty salons



WHY?

Because nothing in the world surpasses Revlon nail enamel... for fabulous color, fashion authority, lasting beauty—and superior quality.

The Committee on Cosmetics of The American Medical Association has accepted Revlon Nail Enamel and other Revlon Products

Revlon *Products Corp., 745 Fifth Avenue, New York, N. Y.*

Bistrimate Tablets (SMITH)

well tolerated, orally effective Systemic Bismuth Therapy with an increasing range of Clinical Effectiveness

Each tablet contains 410 mg. of sodium bismuth triglycollamate, equivalent to 75 mg. of metallic bismuth. Bistrimate rapidly establishes and maintains therapeutically effective excretion levels of bismuth.

Clinical Indications:

Recently published reports reveal that interesting results have been obtained from the clinical use of Bistrimate-Smith in certain dermatological conditions such as lupus erythematosus and lichen planus. Bistrimate may be employed in conjunction with arsenicals in the treatment of all types of syphilis.

Following bibliography which is constantly increasing, and summaries of these reports, are available upon request:

1. Gross, Elmer R., M.D.; Wright, Carroll S., M.D.; Oral Bismuth Therapy in Syphilis and Various Dermatoses—Paper presented at the Pennsylvania Medical Society Meeting, October 8, 1946 at Philadelphia, Pennsylvania.
2. Gross, Elmer R., M.D.; Howles, James K., M.D.; Non-Specific Treatment of Dermatoses and Adjunctive Therapy of Syphilis with Oral Sodium Bismuth Triglycollamate. Read before the Section of Dermatology and Syphilology Meeting of the Centennial Meeting of the A.M.A. at Atlantic City, New Jersey, June 12, 1947.
3. Year Book of Dermatology and Syphilology, 1946, page 31.
4. Sawicky, H. H., M.D.; Bistrimate (sodium bismuth triglycollamate) Administered by Mouth in the Treatment of Chronic Discoid Lupus Erythematosus. The Journal of Investigative Dermatology, vol. 9 #3 September 1947.
5. Howles, James K., M.D.; Treatment of Inflammatory-Dermatoses with Oral Bismuth (sodium bismuth triglycollamate). Southern Medical Journal, vol. 41 #11, pages 1033-1041, November 1948.
6. Pascher, Frances, M.D.; Sawicky, H. H., M.D.; Silverberg, M.G., M.D.; and Emmet, Richard, M.D.; Bistrimate for Lupus Erythematosus, Lichen Planus and other Dermatoses. Journal of Investigative Dermatology, vol. 10, #6, June 1948.
7. Miller, Thomas H., M.D. and Delaney, James R., M.D.; Oral Bismuth therapy in Dermatology. Archives of Dermatology and Syphilology, Vol. 60, August 1949.

CARROLL DUNHAM SMITH
PHARMACAL COMPANY
SERVING GENERATIONS OF PHYSICIANS
New Brunswick, N.J.
Atlanta, Ga.
Chicago, Ill.
Kansas City, Mo.
Los Angeles, Calif.
established 1844

ACCEPTED
COUNCIL ON PHARMACY AND CHEMISTRY
AMERICAN MEDICAL ASSOCIATION